HERCULES Trial

An investigator-driven randomized controlled trial designed to prospectively compare endosuture aneurysm repair (ESAR) to standard endovascular aneurysm repair (EVAR) clinical outcomes in treatment of infrarenal abdominal aortic aneurysm (AAA) in subjects having wide proximal aortic neck diameters (≥ 28 mm and ≤ 32 mm) and meeting device IFU requirements.

You're invested. So are we.

Strength in evidence

HERCULES is designed to collect clinical evidence to better understand the role of ESAR with the Heli-FX™ EndoAnchor™ system in the treatment of challenging wide neck AAA patients.

HERCULES rationale

- EVAR has been established as a safe and effective repair for AAA. However, recent published literature shows wide infrarenal aortic necks are at greater risk for loss of proximal seal and related events.[1-4]

- Recent ANCHOR data shows promising results in treating hostile necks including wide neck anatomy.[5] Higher level evidence will help to further guide treatment algorithms.

- **This trial will provide a foundation to further characterize the clinical outcomes of treatment for patients with infrarenal AAA with wide proximal aortic neck diameters.**

EVAR

Endurant™ II/IIs AAA stent graft system

ESAR

Endurant II/IIs stent graft plus Heli-FX EndoAnchor system

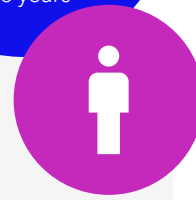
HERCULES design

HERCULES is a post-market, prospective, global, multicenter, randomized (1:1), two-arm, superiority trial designed to compare ESAR to standard EVAR clinical outcomes in treatment of infrarenal AAA in patients having wide proximal aortic neck diameters (≥ 28 mm and ≤ 32 mm).

All imaging-based endpoints will be based on computed tomography angiography (CTA) and analyzed by a core lab. Imaging will be collected for all follow-up time points.

300 patients

Enrolled with one-month, one-year, and annual follow-up through five years



Primary endpoint

Composite of core lab reported data from CT with contrast of freedom from:

1. Type Ia endoleak, and
2. Migration of the proximal portion of the stent graft ≥ 5 mm *(compared to one-month imaging),* and
3. Aneurysm sac growth ≥ 5 mm *(compared to one-month imaging).*

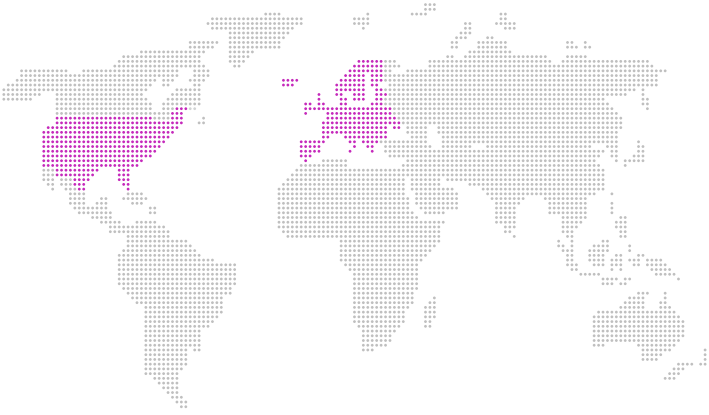
Secondary endpoints

Evaluated using core lab reported data. Freedom from:

- Type Ia endoleak
- Migration of the proximal portion of the stent graft ≥ 5 mm *(compared to one-month imaging)*
- Aneurysm growth ≥ 5 mm *(compared to one-month imaging)*
- Neck dilatation ≥ 3 mm

Up to 40 centers

United States and Europe



Select safety and performance ancillary objectives

- Adequate EndoAnchor penetration (core lab assessed)
- Device-related AEs/SAEs
- Procedure-related AEs through 30 days
- All endoleaks at all timepoints (core lab and site assessed)
- Aneurysm sac changes over time
- Clinically significant migration over time
- Migration ≥ 5 mm and ≥ 10 mm
- Freedom from proximal ring expansion
- Composite of freedom from migration ≥ 5 mm, type Ia, sac growth ≥ 5 mm or neck dilatation ≥ 3 mm at all timepoints

References

[1] Kouvelos GN, et al. *J Cardiovasc Surg*. 2019;60:167-174.
[2] Gargiulo M, et al. *J Vasc Surg*. 2017;66:1065-1072.
[3] McFarland, et al. *J Vasc Surg*. 2019;69:385-393.
[4] Laczynski, Caputo. *J Vasc Surg*. 2021;74:309-315.
[5] Prof. Michel Reijnen. Podium First: ESAR is more than reinforced proximal seal: three-year ANCHOR study results on wide necks and video technique edited case. Presented at: Charing Cross International Symposium; April 26, 2022;London, UK.

Endurant™ II/IIs AAA Stent Graft System

Indications

The Endurant™ II/Endurant™ IIs bifurcated stent grafts are indicated for the endovascular treatment of infrarenal abdominal aortic or aortoiliac aneurysms. They may be utilized in conjunction with the Heli-FX™ EndoAnchor™ system when augmented radial fixation and/or sealing is required; in particular, in the treatment of abdominal aortic aneurysms with short (≥ 4 mm and < 10 mm) infrarenal necks (see Neck length definition below). The Endurant II stent graft system aorto-uni-iliac (AUI) stent graft is indicated for the endovascular treatment of infrarenal abdominal aortic or aortoiliac aneurysms in patients whose anatomy does not allow the use of a bifurcated stent graft. The Endurant II/IIs stent graft system is indicated for use in patients with the following characteristics:

- Adequate iliac or femoral access that is compatible with vascular access techniques, devices, or accessories
- Proximal neck length of
  - ≥ 10 mm; or
  - ≥ 4 mm and < 10 mm when used in conjunction with the Heli-FX EndoAnchor system (bifurcated stent graft only)

  Note: Neck length is defined as the length over which the aortic diameter remains within 10% of the infrarenal diameter.
- Infrarenal neck angulation of ≤ 60°
- Aortic neck diameters with a range of 19 to 32 mm
- Distal fixation length(s) of ≥ 15 mm
- Iliac diameters with a range of 8 to 25 mm
- Morphology suitable for aneurysm repair

Contraindications

The Endurant II/Endurant IIs stent graft system is contraindicated in:

- patients who have a condition that threatens to infect the graft
- patients with known sensitivities or allergies to the device materials

When used with the Heli-FX EndoAnchor system, the Endurant II/IIs stent graft system is also contraindicated in:

- patients with known sensitivities to the EndoAnchor implant materials.

For contraindications regarding ancillary devices used with the Endurant II/Endurant IIs stent graft system, refer to the *Instructions for Use* provided with the device.

Warnings and Precautions

- The long-term safety and effectiveness of the Endurant II/Endurant IIs stent graft system has not been established. All patients should be advised that endovascular treatment requires lifelong, regular follow-up to assess the health and the performance of the implanted endovascular stent graft. Patients with specific clinical findings (e.g., endoleaks, enlarging aneurysms, changes in the structure or position of the endovascular graft), or less than the recommended number of EndoAnchor implants when used in short proximal necks (≥ 4 mm and < 10 mm), should receive enhanced follow-up. Specific follow-up guidelines are described in the *Instructions for Use*.
- Patients experiencing reduced blood flow through the graft limb, aneurysm expansion, and persistent endoleaks may be required to undergo secondary interventions or surgical procedures.

- The Endurant II/Endurant IIs stent graft system is not recommended in patients unable to undergo or who will not be compliant with the necessary preoperative and postoperative imaging and implantation procedures as described in the *Instructions for Use*.
- Renal complications may occur: 1) From an excess use of contrast agents. 2) As a result of emboli or a misplaced stent graft. The radiopaque marker along the edge of the stent graft should be aligned immediately below the lower-most renal arterial origin.
- Studies indicate that the danger of micro-embolization increases with increased procedure duration.
- The safety and effectiveness of the Endurant II/Endurant IIs stent graft system has not been evaluated in some patient populations. Please refer to the product *Instructions for Use* for details.

MRI Safety and Compatibility
Non-clinical testing has demonstrated that the Endurant II/Endurant IIs stent graft is MR Conditional. It can be scanned safely in both 1.5 T and 3.0 T MR systems under certain conditions as described in the product *Instructions for Use*. For additional MRI safety information, please refer to the product *Instructions for Use*.

Adverse Events
Potential adverse events include (arranged in alphabetical order): amputation; anesthetic complications and subsequent attendant problems (e.g., aspiration), aneurysm enlargement; aneurysm rupture and death; aortic damage, including perforation, dissection, bleeding, rupture and death; arterial or venous thrombosis and/or pseudoaneurysm; arteriovenous fistula; bleeding, hematoma or coagulopathy; bowel complications (e.g., ileus, transient ischemia, infarction, necrosis); cardiac complications and subsequent attendant problems (e.g., arrhythmia, myocardial infarction, congestive heart failure, hypotension, hypertension); claudication (e.g., buttock, lower limb); death; edema; EndoAnchor system (for infrarenal EVAR procedures using the Heli-FX EndoAnchor system): partial deployment, inaccurate deployment, fracture, dislodgement, embolization, stent graft damage, modelling balloon damage); embolization (micro and macro) with transient or permanent ischemia or infarction; endoleak; fever and localized inflammation; genitourinary complications and subsequent attendant problems (e.g., ischemia, erosion, femoral-femoral artery thrombosis, fistula, incontinence, hematuria, infection); hepatic failure; impotence; infection of the aneurysm, device access site, including abscess formation, transient fever and pain; lymphatic complications and subsequent attendant problems (e.g., lymph fistula); neurologic local or systemic complications and subsequent attendant problems (e.g., confusion, stroke, transient ischemic attack, paraplegia, paraparesis, paralysis); occlusion of device or native vessel; pulmonary complications and subsequent attendant problems; renal complications and subsequent attendant problems (e.g., artery occlusion, contrast toxicity, insufficiency, failure); stent graft: improper component placement; incomplete component deployment; component migration; suture break; occlusion; infection; stent fracture; graft twisting and/or kinking; insertion and removal difficulties; graft material wear; dilatation; erosion; puncture and perigraft flow; surgical conversion to open repair; vascular access site complications, including infection, pain, hematoma, pseudoaneurysm, arteriovenous fistula, dissection; vascular spasm or vascular trauma (e.g., iliofemoral vessel dissection, bleeding, rupture, death); vessel damage; wound complications and subsequent attendant problems (e.g., dehiscence, infection, hematoma, seroma, cellulitis).

Please reference product Instructions for Use for more information regarding indications, warnings, precautions, contraindications, and adverse events.

Caution
Federal (USA) law restricts this device to sale by or on the order of a physician.

Heli-FX™ EndoAnchor™ System

Indications
The Heli-FX™ EndoAnchor™ system is intended to provide fixation and sealing between endovascular aortic grafts and the native artery. The Heli-FX EndoAnchor system is indicated for use in patients whose endovascular grafts have exhibited migration or endoleak, or are at risk of such complications, in whom augmented radial fixation and/or sealing is required to regain or maintain adequate aneurysm exclusion. The EndoAnchor implant may be implanted at the time of the initial endograft placement, or during a secondary (i.e., repair) procedure.

Contraindications
Treatment with the Heli-FX EndoAnchor system is contraindicated for use in the following circumstances:
- In patients with known allergies to the EndoAnchor implant material (MP35N-LT)
- In conjunction with the Endologix Powerlink™* endograft

Warnings
- The long-term safety and effectiveness of the Endurant II/Endurant IIs stent graft syst
- The long-term performance of the EndoAnchor implant has not been established. All patients should be advised endovascular aneurysm treatment requires long-term, regular follow-up visits to assess the patient's health status and endograft performance.The EndoAnchor implant does not reduce this requirement.
- The EndoAnchor implant and the Heli-FX EndoAnchor system have been evaluated via in vitro testing and determined to be compatible with the Cook Zenith™*, Cook Zenith™* TX2™*, Gore Excluder™*, Gore TAG™*, Medtronic AneuRx™, Medtronic Endurant™, Medtronic Talent™ AAA, Medtronic Talent™ TAA, Medtronic Valiant Xcelerant™, Medtronic Valiant™ Captivia™, and Medtronic Valiant Navion™ endografts. Use with endografts other than those listed above has not been evaluated.
- The performance of the EndoAnchor implant has not been evaluated for securing multiple endograft components together. Not securing EndoAnchor implants into aortic tissue could result in graft fabric damage, component separation, and resultant Type III endoleak
- The performance of the EndoAnchor implant has not been evaluated in vessels other than the aorta. Use of the EndoAnchor implant to secure endografts to other vessels may result in adverse patient consequences such as vascular perforation, bleeding, or damage to adjacent structures.
- The performance of the EndoAnchor implant has not been evaluated for securing multiple anatomical structures together. Such use could result in adverse patient consequences such as vascular perforation, bleeding, or embolic events.

MRI Safety and Compatibility
- The EndoAnchor implants have been determined to be MR Conditional at 3 T or less when the scanner is in Normal Operating Mode with whole-body-averaged SAR of 2 W/kg, or in First Level Controlled Mode with a maximum whole-body-averaged SAR of 4 W/kg.
- Please refer to documentation provided by the endograft system manufacturer for MR safety status of the endograft system with which the EndoAnchor implants are being used.

Potential Adverse Events
Possible adverse events that are associated with the Heli-FX EndoAnchor system, include, but are not limited to:
- Aneurysm rupture
- Death
- EndoAnchor implant embolization
- Endoleaks (Type III)

- Enteric fistula
- Failure to correct/prevent Type I endoleak
- Failure to prevent endograft migration
- Infection
- Renal complications (renal artery occlusion/dissection or contrast-induced acute kidney injury)
- Stroke
- Surgical conversion to open repair
- Vascular access complications, including infection, pain, hematoma, pseudoaneurysm, arteriovenous fistula
- Vessel damage, including dissection, perforation, and spasm

Please reference product Instructions for Use for more information regarding indications, warnings, precautions, contraindications and adverse events. Additional potential adverse events may be associated with endovascular aneurysm repair in general. Refer to the Instructions for Use provided with the endograft for additional potential adverse events.

CAUTION: Federal (USA) law restricts these devices to sale by or on the order of a licensed healthcare practitioner. See package inserts for full product information.

CAUTION: EndoAnchor implant locations should be based upon a detailed examination of the preoperative CT imaging in cases involving irregular or eccentric plaque in the intended sealing zones. EndoAnchor implants should be implanted only into areas of aortic tissue free of calcified plaque or thrombus, or where such pathology is diffuse and less than 2 mm in thickness. Attempting to place EndoAnchor implants into more severe plaque or thrombus may be associated with implantation difficulty and suboptimal endograft fixation and/or sealing.

Not for distribution to patients.

medtronic.com/aortic

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