



Metformin Therapy to Inhibit Progression in Patients with Abdominal Aortic Aneurysm (MetAAA Trial)

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Yu X. et al. Heart 2019

Background

An abdominal aortic aneurysm (AAA), defined as a degenerative enlargement of the (mostly infrarenal) aorta to ≥ 30 mm in diameter, can rapidly lead to death in the event of a sudden vessel rupture. Currently there is no approved drug therapy for abdominal aortic aneurysms. Previous studies (retrospective analyses) have shown that diabetic patients treated with metformin show slower progression rates and are less likely to develop an AAA than non-diabetic patients. This effect is not observed with other anti-diabetic drugs. Thus, metformin seems to be a promising drug to limit AAA progression.

Fujimura N. et al. JVS 2016

Itoga N.K. et al. JVS 2019

Golledge J. et al. BJS 2017

Golledge J. et al. EJVES 2019

Hypothesis

Metformin may provide a conservative treatment option for non-diabetic AAA patients

→ Vienna MetAAA Trial

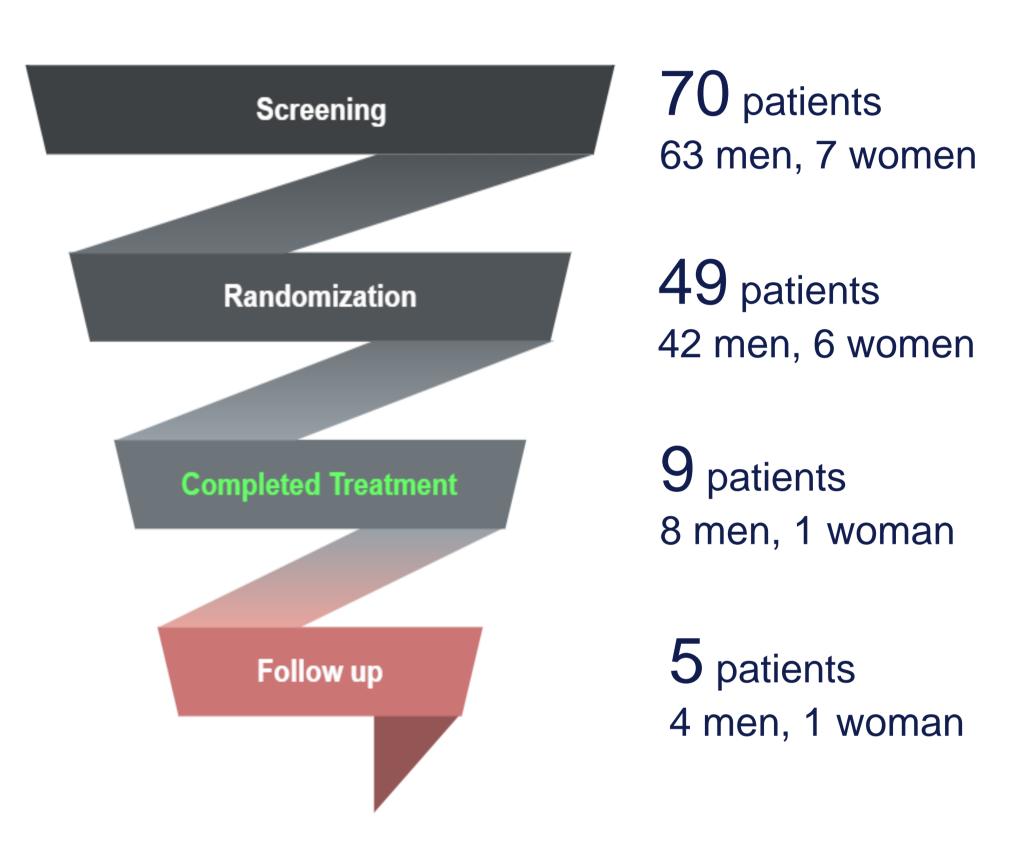
prospective, double-blind, randomized and placebo-controlled safety and efficacy study

Study Design

The MetAAA trial is currently conducting patient recruitment and includes 1 year of metformin therapy and 6 months of follow-up. 170 non-diabetic patients diagnosed with infrarenal AAA Inclusion criteria infrarenal AAA of 3-4.9 cm Pre-screening phase for drug intolerance Exclusion criteria Initial dose: 500 mg 1-0-1 MERCK Glucophage® diabetes Target dose: 1000 mg 1-0-1 indication for surgical AAA repair pregnancy 10% expected drop-out due to drug intolerance 14 days contraindications for metformin Random allocation of patients to metformin and control group eGFR <30 ml/min/1.73m² o liver dysfunction Randomization pancreatitis alcohol abusus Target dose: 1000 mg 1-0-1 MERCK Glucophage® Placebo malnutrition decompensated heart failure Safety endpoints: **Study center:** 12 months Liver dysfunction, reduced kidney function (GFR <30 ml/min/1.73m²) Vienna General Hospital -Indication for surgical AAA repair **Medical University of Vienna** Secondary endpoints Primary endpoint **Enrolment of patients since** 10/2018 AAA growth over 12 months in mm Blood parameters of glucose metabolism, MERCK (diameter and volume) inflammation, neutrophils

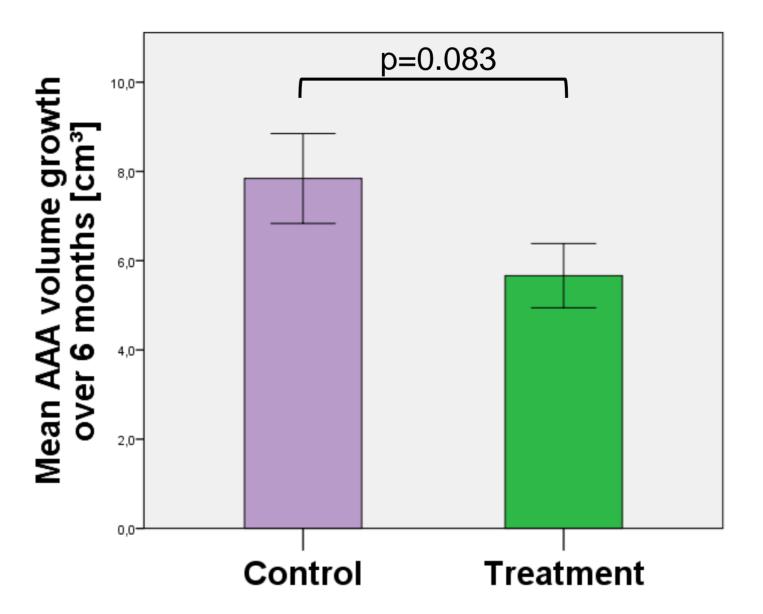
Current Status

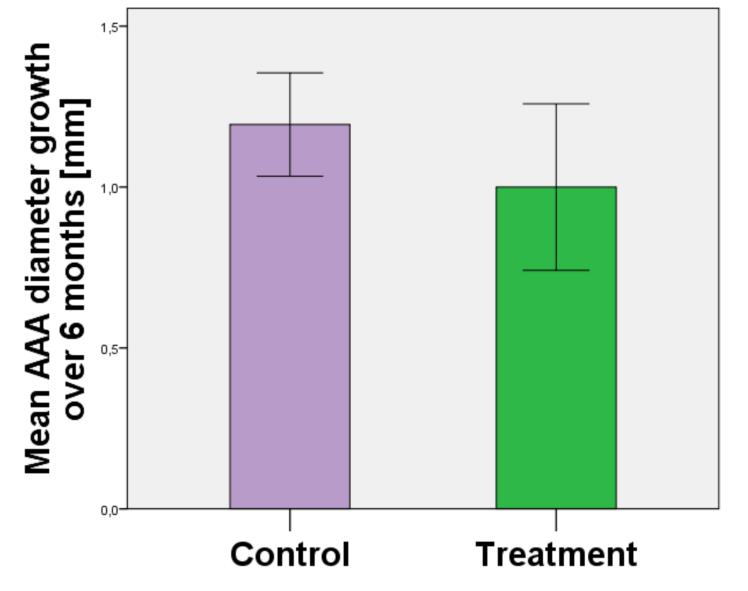
- 21 screening dropouts: mostly gastrointestinal side effects or low kidney function
- 7 treatment dropouts:
 AAA rupture, death, autoimmune disease, withdrawn consent, unspecific side effects
- 6 SAE:
 1 AAA rupture
 2 deaths (cardiac arrest, influenza)
 3 non-elective hospitalizations (resolved w/o sequelae)



Preliminary Data Analysis

12 MetAAA trial patients (blinded) vs 36 historic AAA controls (untreated); matched for baseline AAA diameter (±1.6 mm)





Conclusion & Outlook

- Based on the clinical evidence with diabetic AAA patients, we have initiated a prospective, randomized, double-blind, placebo-controlled trial to demonstrate the efficacy of add-on metformin therapy in non-diabetic AAA patients.
- We aim to establish the first medical treatment to inhibit progression of AAA and thereby possibly reduce the need for major surgery or risk of rupture with the associated mortality, morbidity and cost.