Medizinische Universität Graz

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UNIVERSITÄTSMEDIZIN GÖTTINGEN UMG

Aldosterone Receptor Blockade in **D**iastolic **H**eart **F**ailure

The **Aldo-DHF** Trial

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For the Aldo-DHF Investigators

Registered at *www.controlled-trials.com*: ISCRTN94726526; Eudra-CT no. 2006-002605-31

Disclosures

No disclosures related to this trial.

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Background

Diastolic Heart Failure (DHF, or Heart Failure with Preserved Ejection Fraction) accounts for over 50% of all heart failure cases.

Clinical outcomes are poor in DHF, but no established therapy exists.

Aldosterone has been implicated in the pathogenesis of DHF via aldosterone receptor mediated myocardial fibrosis, hypertrophy, and vascular stiffening.

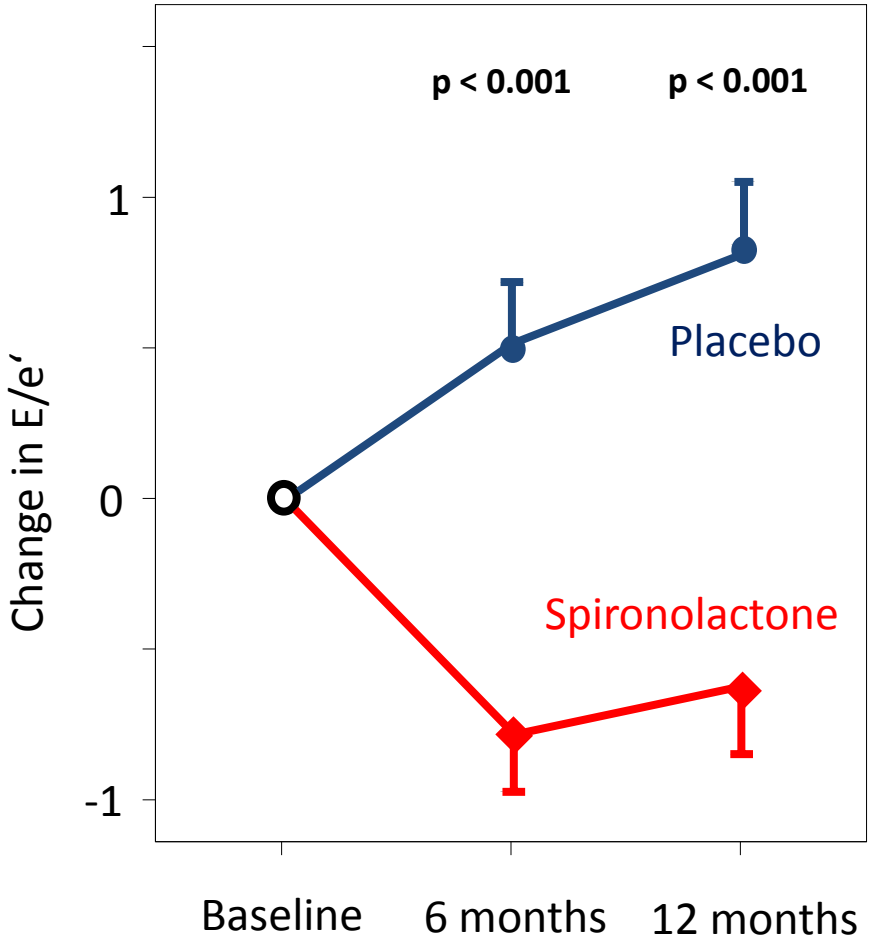
Aldo-DHF was designed to test the efficacy and safety of the aldosterone receptor antagonist Spironolactone in patients with diastolic heart failure.

Aldo-DHF Study Design

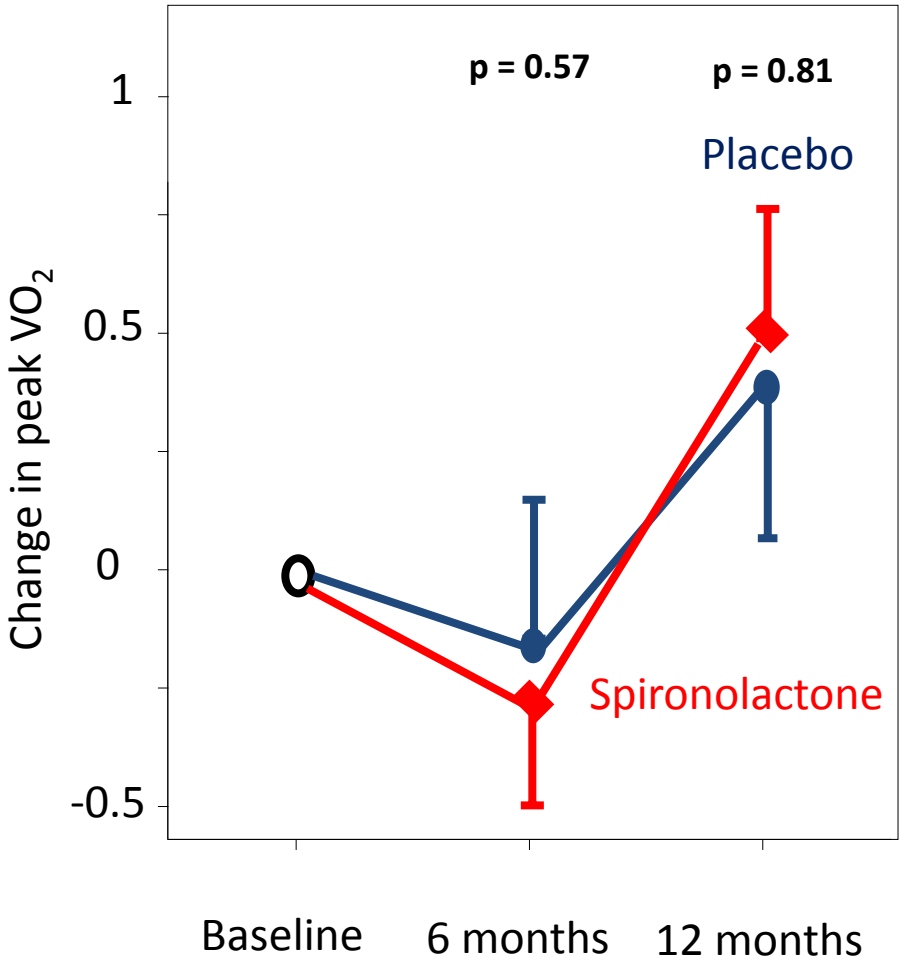
- Multicenter, randomised, placebo-controlled double-blind, two-armed parallel-group study
- Hypothesis: Spironolactone (25 mg) improves cardiac (diastolic) function and exercise capacity as compared to placebo after 1 year of therapy
- Co-Primary endpoints: E/é (echo tissue Doppler derived estimate of filling pressure) and maximal exercise capacity (peak VO_2 on bicycle spiroergometry)
- Key inclusion criteria: Signs/symptoms of heart failure, EF≥50%, evidence of diastolic dysfunction, peak VO_2 <25ml/kg/min
- 422 patients were randomised to Spironolactone or Placebo

Co-Primary endpoints

E/é



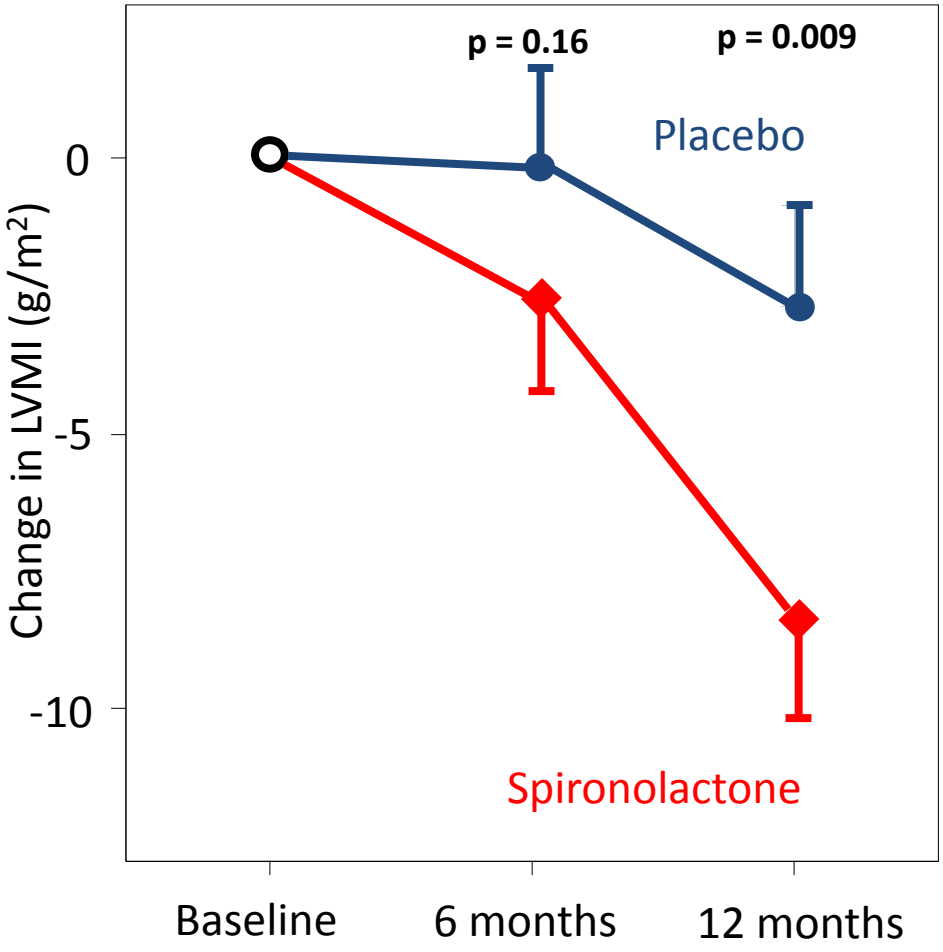
peak VO_2



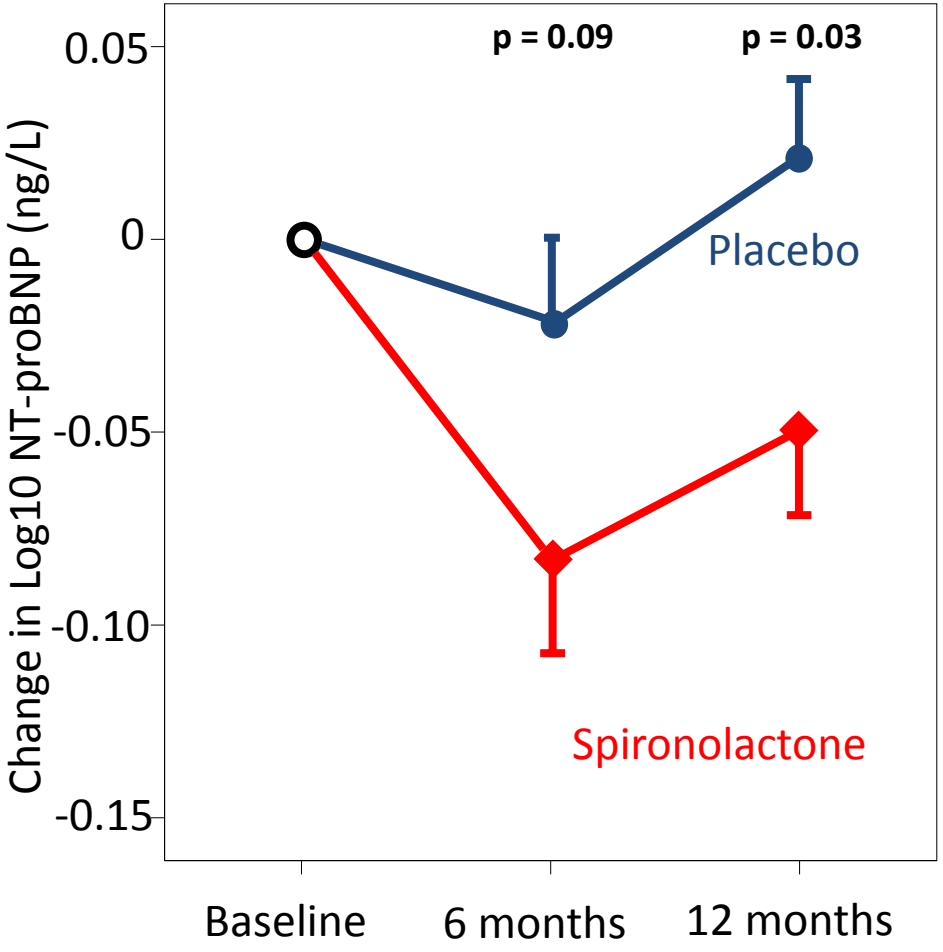
Time since randomisation

Secondary endpoints

Left ventricular mass index



NT-proBNP



Time since randomisation

Safety endpoints: Adverse events

Adverse Events (n,%)	Placebo (n=209)	Spironolactone (n=213)	P-value
Deaths	0 (0)	1 (<1)	1·00
Hospitalisation	50 (24)	60 (28)	0·38
Cardiac	15 (7)	21 (10)	0·38
Non-cardiac	37 (18)	47 (22)	0·27
New/worsening edema	44 (21)	35 (16)	0·26
Worsening renal function	43 (21)	77 (36)	<0·001
eGFR <30 mL/min/1·73m^2 at last visit	1 (<1)	3 (1)	0·62
New/worsening anaemia	18 (9)	34 (16)	0·03
Gynaecomastia	1 (<1)	9 (4)	0·02
Serum potassium			
ever increased >5·0 mmol/L	22 (11)	44 (21)	0·005
ever increased >5·5 mmol/L	3 (1)	4 (2)	1·00

Summary and Conclusions

1. Aldo-DHF is the largest mechanistic Phase IIb trial in DHF
2. Spironolactone (25mg/d) improved diastolic function (E/é), induced structural reverse remodelling (LVMI), and reduced neuroendocrine activation (NT-proBNP)
3. Spironolactone did not improve exercise capacity , NYHA class, or quality of life
4. Spironolactone reduced blood pressure; effects on cardiac structure and function remained significant after adjusting for blood pressure changes
5. Spironolactone was safe and not associated with severe adverse events
6. Spironolactone can be considered in patients with diastolic heart failure for improving cardiac function and blood pressure control