# Two-arm trials of naftidrofuryl oxalate and placebo

#### Kieffer 200165

Study details

Publication type Kieffer 2001,65 full report in peer-reviewed journal

Additional sources of data

Trial design RCT, multicentre

Country France
Dates of participant recruitment NR
Sources of funding NR

Intervention(s) and comparator

Treatment groups Naftidrofuryl oxalate 600 (200 t.i.d.) mg

Comparator Placebo
Run-in phase 4 weeks
Treatment duration 24 weeks

Outcome(s)

Follow-up Baseline, 8 weeks, 16 weeks, 24 weeks

Outcomes and measures MWD: treadmill with constant workload, 3.2 km/hour, 10% incline

PFWD: as MWD

ABPI: mode of measurement NR

Vascular events

AEs: recorded whether or not considered treatment related

Notes on statistics Log transform for walking distances

Population

Eligibility criteria Outpatients of both genders, aged 35–85 years, with moderately severe chronic, stable IC of at least

6 months and which had been clinically stable during the last 3 months and the diagnosis of which was confirmed by arteriography or duplex scan. All patients had already undergone a course of exercise therapy. PFWD and MWD between 100 and 300 m (treadmill 3.2 km/hour, 10% slope), did not vary by more than 25% during placebo run-in phase. Exclude Fontaine stage I, III or IV; non-vascular leg pain; revascularisation within last 6 months or likely to be needed within 6 months; severe or unstable hypertension; exercise-limiting condition or medication; pregnancy or childbearing potential; poor (< 70%) compliance with

medication during placebo run-in

Concomitant interventions allowed

or excluded

Allowed: NR

Disallowed: NR

Power calculation Minimum 100 patients per group required to detect difference of 20% (alpha error 0.5, beta error 0.1) in

treadmill walking distance

 ${\it N}$  randomised to treatments

included in review

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Treatment group	Naftidrofuryl oxalate 200 mg t.i.d.	Placebo
N randomised to treatment	98	98
Baseline characteristics		
Age	Mean 67.5 (SD 10.1) years	Mean 66.3 (SD 10.9) years
Gender	M 78.7%; F 21.3% <sup>a</sup>	M 81.5%; F 18.5%
Smokers	83.1%	89.1%
Diabetics	19.1%	20.6%
Hypertension/blood pressure	51.7%	42.4%
Hyperlipidaemia	35.2%	37.0%
Obesity or weight	BMI mean 25.9 (SD 4.3)	BMI mean 24.5 (SD 3.4)
Angina		,
History of vascular therapy	Prior vascular surgery 25.8%	Prior vascular surgery 22.8%
Other	Hypercholesterolaemia 36.4%	Hypercholesterolaemia 37.0%
Othor	Typotoriolostorolaethia 30.470	Tryper of foliational of 1.0 %
Withdrawals		
Withdrawals/loss to follow-up	Nine randomised to naftidrofuryl oxalate did not supply any more data (five patient refusals, two reported AE, two lost to follow-up). A further 13 withdrew during 6-month study (six patient refusals, four lost to follow-up, three not specified)	Six randomised to placebo did not supply any more data (four patient refusals, one reported AE, one did not meet eligibility criteria). A further 16 withdrew during 6-month study (five patient refusals, six lost to follow-up, five not specified)
Results		
MWD <i>n</i> in analysis	89	92
MWD baseline	Geometric mean 191.9 m, arithmetic mean 202 (SD 62) m	Geometric mean 203.0 m, arithmetic mean 213 (S 63) m
MWD follow-up	At 24 weeks, geometric mean 350.6. Arithmetic means: 16 weeks 322, 24 weeks 385, 32 weeks (2 months without treatment) 296	At 24 weeks, geometric mean 231.1. Arithmetic means: 16 weeks 266, 24 weeks 259, 32 weeks (2 months without treatment) 265
MWD change	At 24 weeks by geometric mean 82.7%. Subgroup geometric means: diabetics 87.2% change, non-diabetics 81.6% change	At 24 weeks by geometric mean 13.9%. Subgroup geometric means: diabetics 9.5% change, non-diabetics 15.0% change
MWD between-group comparison	At 24 weeks by geometric mean $p$ <0.001. Arithmetic means 16 weeks $p$ <0.01, 24 weeks $p$ <0.001 (8 weeks non-significant)	
PFWD <i>n</i> in analysis	89	92
PFWD baseline	Geometric mean 172.3, arithmetic mean 182 (SD 64) m	Geometric mean 177.9, arithmetic mean 189 (SD 63) m
PFWD follow-up	At 24 weeks, geometric mean 330.5. arithmetic means 16 weeks 298, 24 weeks 367, 32 weeks (2 months without treatment) 281	At 24 weeks, geometric mean 207.8. arithmetic means 16 weeks 244, 24 weeks 237, 32 weeks (2 months without treatment) 240
PFWD change	At 24 weeks by geometric mean 91.8%. Subgroup geometric means diabetics 103.0% change, non-diabetics 89.2% change [RM1987 has mean 156.35 (SD 104.88)]	At 24 weeks by geometric mean 16.8%. Subgroup geometric means diabetics 17.3% change, non-diabetics 16.7% change [RM1987 has mean 39.6 (SD 83.84)]
PFWD between-group comparison	At 24 weeks by geometric mean $p$ <0.001. arithmetic 32 weeks (2 months without treatment) $p$ <0.05 (at 8	
ABPI <i>n</i> in analysis	89	92
ABPI baseline	Mean 0.55 (SD 0.35)	Mean 0.55 (SD 0.37)
ABPI follow-up	Mean 0.58 (SD 0.33)	Mean 0.59 (SD 0.33)
ABPI change	Difference 0.03	Difference 0.04
ABPI between-group comparison	Non-significant	

Treatment group	Naftidrofuryl oxalate 200 mg t.i.d.	Placebo
Vascular events <i>n</i> in analysis		
Vascular events follow-up		
Vascular events included		
Vascular events reported	(Two vascular surgery, also listed in AEs)	(Three vascular surgery, also listed in AEs)
Vascular events between-group comparison		
AEs <i>n</i> in analysis	98	98
AEs follow-up		
AEs reported	Number of patients with at least one AE 18. Number of AEs 21 (of which 12 serious: two vascular surgery and two hospitalisation for other diseases and two surgery for other condition). Non-serious possibly treatment-related one mild digestive disorder	Number of patients with at least one AE 21. Number of AEs 25 (of which 13 serious: three vascular surgery and six hospitalisation for other diseases and one surgery for other condition). Non-serious possibly treatment-related — three
AEs between-group comparison	Non-significant	
Mortality reported		
Mortality between-group comparison		
HRQoL <i>n</i> in analysis		
HRQoL baseline		
HRQoL follow-up		
HRQoL change		
HRQoL between-group comparison		

a Figures calculated by reviewer.

### Adhoute 1986<sup>66</sup>

### Study details

Adhoute 1986,66 full report in peer-reviewed journal Publication type

Additional sources of data

Trial design RCT, multicentre

Country France Dates of participant recruitment NR Sources of funding NR

# Intervention(s) and comparator

Treatment groups Naftidrofuryl oxalate 600 (200 t.i.d.) mg

Comparator Placebo

Run-in phase

Treatment duration 24 weeks

Outcome(s)

Follow-up Baseline after 4-week run-in. 3 months. 6 months

PFWD: treadmill with constant workload 3 km/hour, 10% slope Outcomes and measures

ABPI: ultra sonographic measure

AEs: patient self-report

Notes on statistics No adjustment due to homogeneity of groups

Population

Eligibility criteria Patients of both genders between 40 and 70 years with Fontaine stage II PAD, IC for at least 6 months,

> diagnosis confirmed by angiography or Doppler velocimetry examination, PFWD (at 3 km/hour, 10% slope) 150-300 m and after a wash-out period of 1 month up to 20% variation in PFWD. Exclude vascular surgery or specific physical training within 6 months, recent MI, angina pectoris, myocardial/renal/hepatic

insufficiency, labile diabetes, non-treated arterial hypertension

Concomitant interventions allowed

or excluded

Allowed: patients given rules about smoking and physical training

Disallowed: all other treatments for arterial disease

Power calculation NR N randomised to treatments

included in review

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BMI, body mass index; NR, not reported.

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Baseline characteristics         Mean 58.53 (± 8.35) years         Mean 59.62 (± 8.35) years           Gendes         M 69%, F 14%         M 93%; F 7%           Smokers         M 59%, F 14%         M 93%; F 7%           Smokers         Hypertension/bood pressure           Hypertension/bood pressure         Hypertension/bood pressure           Hypertension/bood pressure         Hypertension/bood pressure           Hypertension/bood pressure         Hypertension/bood pressure           Hypertension/bood pressure         4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	Treatment group	Naftidrofuryl oxalate 200 mg t.i.d.	Placebo
Age         Mean 59.53 (± 8.35) years         Mean 59.62 (± 8.35) years           Cenders         M 80%; F 14%         63%           Smokers         63%         63%           Clabetics         Hypertension/bood pressure           Hypertension/bood pressure         Hypertension/bood pressure           Hypertension/bood pressure         Hypertension/bood pressure           History of vascular therapy         Close the control of 154 randomised)           Closely or vascular therapy         (Whole study 118 remained of 154 randomised)           Withdrawals         Natification/ju coaciale group reasons for withdrawal included surgery (n=2), pathology, patient refusal or treatment infolerance (n=2, gasterial)           Placebo group reasons for withdrawal included surgery (n=2), pathology, patient refusal or treatment infolerance (n=2, gasterial)           MWD in analysis         Placebo group censors for withdrawal included surgery (n=2), pathology, patient refusal or treatment infolerance (n=2, gasterial)           MWD between-group comparison         Flags in analysis           MWD between-group comparison         64           FPWD follow-up         355.21 m mean (SD 58.33m)         214.98 m mean (SD 57.92m)           PPWD change         41.24 means (SD 58.33m)         274.24m mean (SD 58.95m)           PPWD between-group comparison         A1.24 meeks 201.37 (SD 29.40) Significantly more improved the proposed pocular policy or p	N randomised to treatment	NR. 64 remained at end of study	NR. 54 remained at end of study
Genders         M 80%; F14%         M 93%; F7%           Smokers         63%         63%           Hyperspension/blood pressure         Hyperspension/blood pressure         Hyperspension/blood pressure         Hyperspension/blood pressure           Hyperspension/blood pressure         Hyperspension/blood pressure         Hyperspension/blood pressure         Hyperspension/blood pressure           Withdrawals         Facure         Facure         Facure           Withdrawals         Withdrawals         Withdrawals         Withdrawals           Withdrawals         Withdrawals         Mediatrolunyl ocalate group reasons for withdrawal included surgery (n=2), pathology, patient refusal or treatment intolerance (n=2, passages or cutaneous rash)         Ference or patient refusal or treatment intolerance (n=2, passages or cutaneous rash)           Results         MMD r in analysis         Mediatrolunyl ocalate group comparison         Ference or cutaneous rash)         Ference or cutaneous rash           PFWD name         214.95m mean (SD 58.33 m)           PFWD brange         214.45m mean (SD 58.33 m)         274.24 m mean (SD 124.55m) at 12 weeks; at 24 weeks 24 mean (SD 124.55m) at 12 weeks; at 24 weeks 24 mean (SD 124.55m) at 12 weeks; at 24 weeks 24 mean (SD 124.55m) at 12 weeks; at 24 weeks 24 mean (SD 124.55m) at 12 weeks 24 weeks 24 mean (SD 124.55m) at 12 weeks 24 weeks 24 mean (SD 124.55m) at 122 we	Baseline characteristics		
Snokers         63%         63%           Diabetics         ************************************	Age	Mean 58.53 (± 8.35) years	Mean 59.62 (±8.35) years
Diabetics         Hyperfinitioadmia         31%         33%           Loseily or veight         37%         33%           Angina         History of vascular therapy         History of vascular therapy           Other         Withdrawals         Withdrawals           Withdrawals/loss to follow-up Allow-up Races to place on proper peasons for withdrawal included surgery (n=2), pathology, patient refusal or treatment intolerance (n=2, assistagles) Place to group reasons for withdrawal included surgery (n=3), pathology, patient refusal or treatment intolerance (n=2, anusea or cutaneous rash)           Results         MWD n in analysis         4	Genders	M 86%; F 14%	M 93%; F 7%
HyperIndisation 1         31%         33%           Obesity or weight         4         4           Angina         4         4           History of vascular therapy         6         4           Other         4         Activationary (Withdrawals)           Withdrawals         4         Activationary oxalate group reasons for withdrawal included surgery (n=2), pathology, patient refusal or treatment intolerance (n=2, austea) or cutaneous rash)         4           Results         4         4           MWD n in analysis         4         5           MWD baseline         4         4           MWD brown-group comparison         214,95m mean (SD 58,33m)         214,99m mean (SD 57,92m)           PFWD n in analysis         4         24 weeks 416.36 (SD 273,58) m         214,242 m mean (SD 157,92m)           PFWD passeline         214,95m mean (SD 193,11 m) at 12 weeks; at 2424 m mean (SD 159,150 m)         24 weeks 313.01 (SD 169,56) m)           PFWD follow-up         335,21 m mean (SD 193,11 m) at 12 weeks; at 2424 m mean (SD 169,56) m)         24 weeks 313.01 (SD 169,56) m)           PFWD change         4 12 weeks 201,37 (SD 254,80) significantly more improved than placabo ρ < 0.05; at 24 weeks antidrofruryl oxalate significantly more improved than placabo ρ < 0.05; at 24 weeks antidrofruryl oxalate significantly more improved than placabo ρ < 0.05; at 24 weeks antidrofruryl oxalate significantly more i		63%	63%
Pyentiplidaemia       31%       33%         Obesity or weight         Angina         History of vascular therapy         Withdrawals         Withdrawals/loss to follow-up       (Whole study 118 remained of 154 randomised)         Withdrawals/loss to follow-up       (Whole study 118 remained of 154 randomised)         National Problems of the study 118 remained of 154 randomised)         National Problems of the study 118 remained of 154 randomised)         National Problems of the study 118 remained of 154 randomised)         National Problems of the study 118 remained of 154 randomised)         National Problems of the study 118 remained of 154 randomised)         National Problems of the study 118 remained of 154 randomised)         National Problems of the study 118 remained of 154 randomised)         National Problems of the study 118 remained of 154 randomised)         National Problems of the study 118 remained of 154 randomised)         National Problems of the study 118 remained of 154 randomised)         National Problems of the study 118 remained of 154 randomised)         National Problems of the study 118 remained of 154 randomised         National Problems of the study 118 remained of 154 randomised	Diabetics		
Obesity or weight       Angina         History of vascular therapy       History of vascular therapy         Other       Withdrawals         Withdrawals/oss to follow-up       (Whole study 118 remained of 154 randomised)         Nafitorfouryl oxalate group reasons for withdrawal included surgery (n=2), pathology, patient refusal or treatment intolerance (n=2, gastralgia)         Placebo group reasons for withdrawal included surgery (n=3), pathology, patient refusal or treatment intolerance (n=2, nausea or cutaneous rash)         Results         MWD n in analysis         MWD to ange         MWD baseline       44 95 m mean (SD 58.33 m)       214.98 m mean (SD 57.92 m)         PFWD follow-up       338 21 m mean (SD 193.11 m) at 12 week; at 24 weeks 41.30 (SD 148.50 m) at 12 weeks; at 24 weeks 41.30 (SD 148.50 m) at 12 weeks; at 24 weeks 41.30 (SD 148.50 m)       244 weeks 41.30 (SD 148.50 m) at 12 weeks; at 24 weeks 41.30 (SD 148.50 m)         PFWD change       At 24 weeks 201.37 (SD 254.80) significantly improved p < 0.02; [RM1987 has mean 196.54 (SD 122.60)]			
Arigina History of vascular therapy Other  Withdrawals		31%	33%
History of vascular therapy Other  ###################################	, ,		
Withdrawals       Withdrawals/loss to follow-up     (Whole study 118 remained of 154 randomised)     Natitidrofuny loxalate group reasons for withdrawal included surgery (n=2), pathology, patient refusal or treatment intolerance (n=3, gastralgia)       Placebo group reasons for withdrawal included surgery (n=3), pathology, patient refusal or treatment intolerance (n=2, nausea or cutaneous rash)       Results       MWD n in analysis       MWD baseline     4       MWD baseline     54       PFWD n in analysis     64       PFWD paseline     214.95m mean (SD 58.33m)       PFWD prior (s)     335.21m mean (SD 58.33m)       PFWD follow-up     335.21m mean (SD 193.11m) at 12 weeks; at 24 weeks 416.36 (SD 273.58) m       PFWD change     A1 24 weeks 201.37 (SD 264.80) significantly improved p<0.002; [RM1987 has mean 199.63 (SD 279.91)]			
Withdrawals         Withdrawals/loss to follow-up       (Whole study 118 remained of 154 randomised)			
Withdrawals/loss to follow-up  Withdrawals/loss to follow-up  Naftidrofuryl oxalate group reasons for withdrawal included surgery (n=2), pathology, patient refusal or treatment intolerance (n=2, gastralgia)  Placebog group reasons for withdrawal included surgery (n=3), pathology, patient refusal or treatment intolerance (n=2, nausea or cutaneous rash)  Results  MWD n in analysis  MWD baseline  MWD follow-up  MWD change  MWD between-group comparison  PPWD baseline  214.95m mean (SD 58.33m)  214.95m mean (SD 57.92 m)  PPWD follow-up  335.21 m mean (SD 58.33m)  244 weeks 313.01 (SD 169.96) m  274.24 m mean (SD 17.92 m)  PPWD change  At 24 weeks 201.37 (SD 254.80) significantly improved po.0.02; [RM1987 has mean 199.63 (SD 182.66)]  PPWD between-group comparison  At 12 weeks naftidrofuryl oxalate significantly more improved than placebo p < 0.05; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo p < 0.05; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo p < 0.00.  ABPI n in analysis  ABPI baseline  0.65 (SD 0.24)  0.61 (SD 0.20)  ABPI follow-up  0.67 (SD 0.23)  0.62 (SD 0.17)  ABPI between-group comparison  Non-significant  Non-significant  Non-significant  Vascular events n in analysis  Vascular events reported  Vascular events between-group	Other		
Naftidrofuryl oxalate group reasons for withdrawal included surgery (n=2), pathology, patient refusal or treatment intolerance (n=3, gastralgia) Placebo group reasons for withdrawal included surgery (n=3), pathology, patient refusal or treatment intolerance (n=2, nausea or cutaneous rash)  **Results**  MWD n in analysis  MWD baseline  MWD follow-up  MWD change  MWD between-group comparison  PPWD n in analysis  64  54  PPWD n in analysis  64  PPWD n in analysis  64  PPWD between-group comparison  PPWD change  At 24 weeks 416.36 (SD 273.58) m  pPWD change  At 24 weeks 201.37 (SD 254.80) significantly improved p < 0.02; [RM1987' has mean 199.63 (SD 273.58) m  prewD between-group comparison  At 24 weeks attication with a significantly more improved than placebo p < 0.05; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo p < 0.05; at 24 weeks antidrofuryl oxalate significantly more improved than placebo p < 0.05; at 24 weeks antidrofuryl oxalate significantly more improved than placebo p < 0.05; at 24 weeks antidrofuryl oxalate significantly more improved than placebo p < 0.05; at 24 weeks antidrofuryl oxalate significantly more improved than placebo p < 0.05; at 24 weeks antidrofuryl oxalate significantly more improved than placebo p < 0.05; at 24 weeks antidrofuryl oxalate significantly more improved than placebo p < 0.05; at 24 weeks antidrofuryl oxalate significantly more improved than placebo p < 0.05; at 24 weeks antidrofuryl oxalate significantly more improved than placebo p < 0.05; at 24 weeks antidrofuryl oxalate significantly more improved than placebo p < 0.05; at 24 weeks antidrofuryl oxalate significantly more improved than placebo p < 0.05; at 24 weeks antidrofuryl oxalate significantly more improved than placebo p < 0.05; at 24 weeks antidrofuryl oxalate significantly more improved than placebo p < 0.05; at 24 weeks antidrofuryl oxalate significantly more improved than placebo p < 0.05; at 24 weeks antidrofuryl oxalate significantly more improved than placebo p < 0.05; at 24 w	Withdrawals		
treatment intolerance ( $n=3$ , gastraligia)  Results  MWD $n$ in analysis  MWD $n$ in analysis  MWD baseline  MWD follow-up  MWD between-group comparison  FPWD $n$ in analysis  64  FPWD $n$ in analysis  64  FPWD $n$ in analysis  64  FPWD baseline  MYD baseline  At 24 weeks 201.37 (SD 254.80) significantly more improved than placebo $p < 0.05$ ; at 24 weeks aftlidrightly oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks aftleforty oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks aftleforty oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks aftleforty oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks aftleforty oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks aftleforty oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks aftleforty oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks aftleforty oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks aftleforty oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks aftleforty oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks aftleforty oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks aftleforty oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks aftleforty oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks aftleforty oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks aftleforty oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks aftleforty oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks aftleforty oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks aftleforty oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks aftleforty oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks aftleforty oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks aftle	Withdrawals/loss to follow-up	(Whole study 118 remained of 154 randomised)	
Intolerance (n = 2, nausea or cutaneous rash)			luded surgery ( $n=2$ ), pathology, patient refusal or
MWD rin analysis MWD baseline MWD follow-up MWD change MWD between-group comparison  FPWD n in analysis 64 FPWD n in analysis 64 FPWD baseline 214.95 m mean (SD 58.33 m) 214.98 m mean (SD 57.92 m) PFWD follow-up 335.21 m mean (SD 193.11 m) at 12 weeks; at 24 weeks 131.31 (SD 169.56) m At 24 weeks 210.37 (SD 254.80) significantly improved p<0.02; [RM1987 has mean 199.63 (SD 247.911)]  PFWD between-group comparison At 12 weeks antidrofuryl oxalate significantly more improved than placebo p<0.02; [RM1987 has mean 106.54 (SD 182.66)]  ABPI n in analysis  ABPI baseline 0.65 (SD 0.24) 0.67 (SD 0.23) 0.62 (SD 0.17) ABPI change Non-significant ABPI between-group comparison Non-significant Vascular events n in analysis Vascular events n in analysis Vascular events follow-up Vascular events follow-up Vascular events follow-up Vascular events included Vascular events between-group			ry ( $n$ =3), pathology, patient refusal or treatment
MWD baseline MWD follow-up MWD change MWD between-group comparison  FFWD n in analysis  64  FFWD n in analysis  64  FFWD baseline  214.95 m mean (\$D 58.33 m)  214.98 m mean (\$D 57.92 m)  214.98 m me	Results		
MWD follow-up           MWD change           MWD between-group comparison           PFWD n in analysis         64         54           PFWD baseline         214.95 m mean (SD 58.33 m)         214.98 m mean (SD 57.92 m)           PFWD follow-up         335.21 m mean (SD 193.11 m) at 12 weeks; at 24 weeks 313.01 (SD 169.56) m         224 weeks 416.36 (SD 273.58) m         224 weeks 313.01 (SD 169.56) m           PFWD change         At 24 weeks 201.37 (SD 254.80) significantly improved p < 0.02; [RM1987 has mean 199.63 (SD 247.91)]	MWD <i>n</i> in analysis		
MWD change  MWD between-group comparison  PFWD n in analysis  64  FFWD baseline  214.95 m mean (SD 58.33 m)  214.98 m mean (SD 57.92 m)  PFWD follow-up  335.21 m mean (SD 193.11 m) at 12 weeks; at 24 weeks 313.01 (SD 169.56) m  PFWD change  At 24 weeks 201.37 (SD 254.80) significantly improved p < 0.02; [RM1987 has mean 199.63 (SD 247.91)]  PFWD between-group comparison  At 12 weeks naftidrofuryl oxalate significantly more improved than placebo p < 0.02; [RM1987 has mean 199.63 (SD 182.66)]  PFWD between-group comparison  At 12 weeks naftidrofuryl oxalate significantly more improved than placebo p < 0.05; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo p < 0.05  ABPI n in analysis  ABPI baseline  0.65 (SD 0.24)  0.67 (SD 0.23)  ABPI change  Non-significant  Non-significant  Non-significant  Vascular events n in analysis  Vascular events follow-up  Vascular events follow-up  Vascular events reported  Vascular events reported  Vascular events between-group	MWD baseline		
MWD between-group comparison  PFWD $n$ in analysis 64  PFWD baseline 214.95 m mean (SD 58.33 m) 214.98 m mean (SD 57.92 m)  PFWD follow-up 335.21 m mean (SD 193.11 m) at 12 weeks; at 24 weeks 416.36 (SD 273.58) m 24 weeks 313.01 (SD 169.56) m  PFWD change At 24 weeks 201.37 (SD 254.80) significantly improved $p < 0.02$ ; [RM1987 has mean 199.63 (SD 182.66)]  PFWD between-group comparison At 12 weeks naftidrofuryl oxalate significantly more improved than placebo $p < 0.02$ ; [RM1987 has mean 199.63 (SD 182.66)]  PFWD between-group comparison At 12 weeks naftidrofuryl oxalate significantly more improved than placebo $p < 0.02$ ; [RM1987 has mean 106.54 (SD 182.66)]  PFWD between-group comparison At 12 weeks naftidrofuryl oxalate significantly more improved than placebo $p < 0.02$ ; [RM1987 has mean 106.54 (SD 182.66)]  PFWD between-group comparison At 12 weeks naftidrofuryl oxalate significantly more improved than placebo $p < 0.02$ ; [RM1987 has mean 106.54 (SD 182.66)]  PFWD between-group comparison At 12 weeks naftidrofuryl oxalate significantly more improved than placebo $p < 0.02$ ; [RM1987 has mean 106.54 (SD 182.66)]  PFWD between-group comparison At 12 weeks naftidrofuryl oxalate significantly more improved than placebo $p < 0.02$ ; [RM1987 has mean 106.54 (SD 182.66)]  PFWD between-group comparison At 12 weeks naftidrofuryl oxalate significantly more improved than placebo $p < 0.02$ ; [RM1987 has mean 106.54 (SD 182.66)]  PFWD between-group comparison At 24 weeks 98.33 (SD 145.65) significantly improved $p < 0.02$ ; [RM1987 has mean 199.63 (SD 182.66)]  PFWD between-group comparison At 24 weeks 98.33 (SD 145.65) significantly improved $p < 0.02$ ; [RM1987 has mean 199.63 (SD 182.66)]  PFWD between-group comparison At 24 weeks 98.33 (SD 145.65) significantly improved $p < 0.02$ ; [RM1987 has mean 199.63 (SD 182.66)]  PFWD between-group comparison At 24 weeks 98.33 (SD 145.65) significantly improved $p < 0.02$ ; [RM1987 has mean 199.63 (SD 182.66)]  PFWD between-group comparison At 24 weeks 98.33 (SD 145.65) signific	MWD follow-up		
PFWD n in analysis 64 54 PFWD baseline 214.95 m mean (SD 58.33 m) 214.98 m mean (SD 57.92 m) PFWD follow-up 335.21 m mean (SD 193.11 m) at 12 weeks; at 24 weeks 416.36 (SD 273.58) m 24 weeks 313.01 (SD 169.56) m PFWD change At 24 weeks 201.37 (SD 254.80) significantly improved p < 0.02; [RM1987 has mean 199.63 (SD 247.91)] At 24 weeks 98.33 (SD 145.65) significantly improved p < 0.02; [RM1987 has mean 199.63 (SD 247.91)] At 24 weeks 98.33 (SD 145.65) significantly improved p < 0.02; [RM1987 has mean 199.63 (SD 247.91)] At 25 weeks naftidrofuryl oxalate significantly more improved than placebo p < 0.02; [RM1987 has mean 106.54 (SD 182.66)] At 12 weeks naftidrofuryl oxalate significantly more improved than placebo p < 0.05; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo p < 0.02  ABPI n in analysis ABPI baseline 0.65 (SD 0.24) 0.61 (SD 0.20) ABPI follow-up 0.67 (SD 0.23) 0.62 (SD 0.17) ABPI change Non-significant Non-significant ABPI between-group comparison Non-significant  Vascular events n in analysis Vascular events follow-up Vascular events follow-up Vascular events reported Vascular events between-group	MWD change		
PFWD baseline 214.95 m mean (SD 58.33 m) 214.98 m mean (SD 57.92 m) PFWD follow-up 335.21 m mean (SD 193.11 m) at 12 weeks; at 24 weeks 416.36 (SD 273.58) m 24 weeks 313.01 (SD 169.56) m PFWD change At 24 weeks 201.37 (SD 254.80) significantly improved $\rho < 0.02$ ; [RM1987 has mean 199.63 (SD 247.91)] At 12 weeks naftidrofuryl oxalate significantly more improved than placebo $\rho < 0.02$ ; [RM1987 has mean 106.54 (SD 182.66)] PFWD between-group comparison At 12 weeks naftidrofuryl oxalate significantly more improved than placebo $\rho < 0.02$ ; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo $\rho < 0.02$ ; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo $\rho < 0.02$ ; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo $\rho < 0.02$ .  ABPI $\rho = 0.02$ $\rho $	MWD between-group comparison		
PFWD baseline 214.95 m mean (SD 58.33 m) 214.98 m mean (SD 57.92 m) PFWD follow-up 335.21 m mean (SD 193.11 m) at 12 weeks; at 24 weeks 416.36 (SD 273.58) m 24 weeks 313.01 (SD 169.56) m PFWD change At 24 weeks 201.37 (SD 254.80) significantly improved $\rho < 0.02$ ; [RM1987 has mean 199.63 (SD 247.91)] At 12 weeks naftidrofuryl oxalate significantly more improved than placebo $\rho < 0.02$ ; [RM1987 has mean 106.54 (SD 182.66)] PFWD between-group comparison At 12 weeks naftidrofuryl oxalate significantly more improved than placebo $\rho < 0.02$ ; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo $\rho < 0.02$ ; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo $\rho < 0.02$ ; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo $\rho < 0.02$ .  ABPI $\rho = 0.02$ $\rho $			
PFWD follow-up  335.21 m mean (SD 193.11 m) at 12 weeks; at 24 weeks 313.01 (SD 124.55 m) at 12 weeks; at 24 weeks 416.36 (SD 273.58) m  PFWD change  At 24 weeks 201.37 (SD 254.80) significantly improved \$p < 0.02; [RM1987 has mean 199.63 (SD 247.91)]  PFWD between-group comparison  At 12 weeks naftidrofuryl oxalate significantly more improved than placebo \$p < 0.02; [RM1987 has mean 106.54 (SD 182.66)]  ABPI \$n\$ in analysis  ABPI baseline  0.65 (SD 0.24)  ABPI follow-up  0.67 (SD 0.23)  ABPI between-group comparison  Non-significant  Vascular events \$n\$ in analysis  Vascular events follow-up  Vascular events follow-up  Vascular events follow-up  Vascular events between-group  Vascular events between-group		• .	
PFWD change   At 24 weeks 416.36 (SD 273.58) m		·	· · · · · · · · · · · · · · · · · · ·
improved $p < 0.02$ ; [RM1987 has mean 199.63 (SD improved $p < 0.02$ ; [RM1987 has mean 106.54 (SD 247.91)]  PFWD between-group comparison  At 12 weeks naftidrofuryl oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo $p < 0.05$ (SD 0.62 (SD 0.17)  ABPI to 0.65 (SD 0.24)  0.61 (SD 0.20)  0.62 (SD 0.17)  Non-significant  Vascular events $p = 0.05$ (SD 0.23)  Non-significant  Vascular events $p = 0.05$ (SD 0.23)  Non-significant  Vascular events $p = 0.05$ (SD 0.23)  Non-significa	PFWD follow-up	,	, , , , , , , , , , , , , , , , , , , ,
PFWD between-group comparison At 12 weeks naftidrofuryl oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo $p < 0.05$ ; at 24 weeks naftidrofuryl oxalate significantly more improved than placebo $p < 0.02$ ABPI $n$ in analysis  ABPI baseline 0.65 (SD 0.24) 0.61 (SD 0.20)  ABPI follow-up 0.67 (SD 0.23) 0.62 (SD 0.17)  ABPI change Non-significant Non-significant  ABPI between-group comparison Non-significant  Vascular events $n$ in analysis  Vascular events follow-up  Vascular events included  Vascular events reported  Vascular events between-group	PFWD change		
naftidrofuryl oxalate significantly more improved than placebo $p < 0.02$ ABPI $n$ in analysis  ABPI baseline 0.65 (SD 0.24) 0.61 (SD 0.20)  ABPI follow-up 0.67 (SD 0.23) 0.62 (SD 0.17)  ABPI change Non-significant Non-significant  ABPI between-group comparison Non-significant  Vascular events $n$ in analysis  Vascular events follow-up  Vascular events included  Vascular events reported  Vascular events between-group			
ABPI baseline 0.65 (SD 0.24) 0.61 (SD 0.20)  ABPI follow-up 0.67 (SD 0.23) 0.62 (SD 0.17)  ABPI change Non-significant Non-significant  ABPI between-group comparison Non-significant  Vascular events n in analysis  Vascular events follow-up  Vascular events included  Vascular events reported  Vascular events between-group	PFWD between-group comparison		
ABPI follow-up  ABPI change  Non-significant  ABPI between-group comparison  Vascular events n in analysis  Vascular events follow-up  Vascular events reported  Vascular events between-group	ABPI <i>n</i> in analysis		
ABPI follow-up  ABPI change  Non-significant  ABPI between-group comparison  Vascular events n in analysis  Vascular events follow-up  Vascular events reported  Vascular events between-group	ABPI baseline	0.65 (SD 0.24)	0.61 (SD 0.20)
ABPI between-group comparison Non-significant  Vascular events n in analysis  Vascular events follow-up  Vascular events included  Vascular events reported  Vascular events between-group	ABPI follow-up		
Vascular events <i>n</i> in analysis  Vascular events follow-up  Vascular events included  Vascular events reported  Vascular events between-group	ABPI change	Non-significant	Non-significant
Vascular events follow-up Vascular events included Vascular events reported Vascular events between-group	ABPI between-group comparison	Non-significant	
Vascular events included  Vascular events reported  Vascular events between-group	Vascular events <i>n</i> in analysis		
Vascular events reported Vascular events between-group	Vascular events follow-up		
Vascular events between-group	Vascular events included		
	Vascular events reported		
	· .		

Treatment group	Naftidrofuryl oxalate 200 mg t.i.d.	Placebo
AEs <i>n</i> in analysis	64	54
AEs follow-up		
AEs reported	Gastric, 5	Gastric, 6
AEs between-group comparison		
Mortality reported	One death due to MI. Does not specify if during	ng run-in period, or, if randomised, to which group
Mortality between-group comparison		
HRQoL <i>n</i> in analysis		
HRQoL baseline		
HRQoL follow-up		
HRQoL change		
HRQoL between-group comparison		

## Trubestein 1984<sup>67</sup>

Study details

Publication type Trubestein 1984,67 full report in peer-reviewed journal

Additional sources of data de Backer-Tine 2008 (RM1987)<sup>32</sup>

Trial design RCT, multicentre
Country Germany
Dates of participant recruitment 1981–3
Sources of funding NR

Intervention(s) and comparator

Treatment groups Naftidrofuryl oxalate 600 (200 t.i.d.) mg

Comparator Placebo
Run-in phase 4 weeks
Treatment duration 12 weeks

Outcome(s)

Follow-up Baseline, 8 and 12 weeks

Outcomes and measures MWD: treadmill with constant workload 5 km/hour, 10% slope. Performed twice with at least 20 minutes

interval

PFWD: as MWD

ABPI: Doppler ultrasound (venous occlusion plethysmography)

AEs: method of data collection not reported

Notes on statistics Log transform for MWD and PFWD

Population

Eligibility criteria IC patients between 40 and 65 years, PAD of femoral artery, with IC for at least 6 months and maximum

5 years, no physical training for at least 6 months, diagnosis confirmed with angiography, baseline PFWD (at 5 km/hour, 10% slope) of 100–300 m, after 4-week run-in no more than 30% change. Exclude beta-blockers, defibrinogenating enzymes, antiplatelets, anticoagulants; non-vascular exercise limiting diseases, coronary heart disease within 6 months, myocardial/respiratory/renal insufficiency, severe hypertension

systolic 180 mmHg, diastolic 110 mmHg, vascular surgery within 6 months

Concomitant interventions allowed

or excluded

Allowed: therapy allowed

Disallowed: beta-blockers, defibrinogenating enzymes, antiplatelets, anticoagulants

Power calculation

N randomised to treatments

included in review

104

Treatment group	Naftidrofuryl oxalate 200 mg t.i.d.	Placebo
N randomised to treatment	54	50
Baseline characteristics		
Age		
Gender		
Smokers	63%	44%
Diabetics		
Hypertension/blood pressure		
Hyperlipidaemia		
Obesity or weight		
Angina		
History of vascular therapy		
Other		
Withdrawals		
Withdrawals/loss to follow-up		
Results		
MWD <i>n</i> in analysis	54	50
MWD baseline	220 m	224 m
MWD follow-up	342 m	314 m
MWD change		
MWD between-group comparison	Non-significant between groups. For subgroup stends significantly more improvement than placebo $p < 0.0$ or tibial arteries	sis femoral artery, naftidrofuryl oxalate group 2; non-significant between groups for occlusion femoral
PFWD <i>n</i> in analysis	54	50
PFWD baseline	137 m	135 m
PFWD follow-up	230 m	171 m
PFWD change	Difference 93 m [de Backer-Tine <sup>32</sup> mean 82.2 (SD 144.39)]	Difference 36 m [de Backer-Tine <sup>32</sup> mean 32.48 (SD 68.49)]
PFWD between-group comparison	p<0.02. For subgroups stenosis femoral artery and significantly more improvement than placebo $p$ <0.0 femoral artery; tibial arteries	
ABPI <i>n</i> in analysis	54	50
ABPI baseline	98 (SD 3.7) mmHg [unclear if mean and SD]	93 (SD 3.2) mmHg
ABPI follow-up	101 (SD 3.98) mmHg (non-significant)	92 (SD 3.9) mmHg (non-significant)
ABPI change		
ABPI between-group comparison	Non-significant change for either group	
Vascular events <i>n</i> in analysis		
Vascular events follow-up		
Vascular events included		
Vascular events reported		
Vascular events between-group comparison		

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Treatment group	Naftidrofuryl oxalate 200 mg t.i.d.	Placebo
AEs <i>n</i> in analysis	54	50
AEs follow-up		
AEs reported	n=2 gastric disorders or erythema	n=2 gastric disorders or erythema
AEs between-group comparison		
Mortality reported		
Mortality between-group comparison		
HRQoL <i>n</i> in analysis		
HRQoL baseline		
HRQoL follow-up		
HRQoL change		
HRQoL between-group comparison		

#### Spengel 200247

### Study details

Publication type Spengel 2002,47 full report in peer-reviewed journal

Additional sources of data

Trial design Meta-analysis of three multicentre RCTs (Liard 1997, Spengel 1999 and D'Hooge 2001)

Country Germany, France, Belgium

Dates of participant recruitment NR Sources of funding NR

### Intervention(s) and comparator

Treatment groups Naftidrofuryl oxalate 600 (200 t.i.d.) mg

Comparator Placebo
Run-in phase 1 month
Treatment duration 24 weeks

#### Outcome(s)

Follow-up Baseline, 12 and 24 weeks

Outcomes and measures PFWD: Claudication distance as estimated by patient at baseline and at the end of the study

AEs: AEs were reported by the patients, in response to indirect questions from the investigator, who

assessed their relationship to treatment. Reported as death, serious, minor

HRQoL: CLAU-S (five dimensions – daily living, pain, social life, disease-specific anxiety, mood)

Notes on statistics Individual patient data meta analysis, study block factor added. Many other technical details reported

CLAU-S multivariate analysis of covariance using the five dimensions at baseline as the multivariate covariate. If this showed effect, univariate analysis of covariance conducted. Multivariate analysis of covariance adjusted for baseline values, study effect and first order study treatment interaction

#### Population

Eligibility criteria IC (Fontaine stage II), age 40–80 years, history of IC > 3 months, stable over the previous 3 months,

subjective PFWD of 50– $500\,\text{m}$ , ABPI of  $\leq$  0.85. In addition, it is not clear if only patients who completed the 1-month run-in (included those who had not undergone any surgical intervention during the previous 3 months nor was any surgical intervention planned and that they did not have any difficulty in understanding, or completing the questionnaire) and patients whose ABPI remained  $\leq$  0.85 and whose tablet

compliance was > 70% were randomised

Concomitant interventions allowed

or excluded

NR for trial, though some patients excluded for taking non-permitted concomitant medication. For run-in period, no concomitant treatment with vasoactive or rheologically active substances was permitted, basic rules pertaining to hygiene, diet, tobacco consumption and physical exercise were explained to the patients

Power calculation NR

N randomised to treatments

included in review

754

Treatment group	Naftidrofuryl oxalate 200 mg t.i.d.	Placebo
N randomised to treatment	382	372
Baseline characteristics		
Age (years)	Mean 66.2 ± 9.5	Mean 65.7 ± 9.1
Gender	M, 70.4%; F, 29.6%	M, 73.8%; F, 26.2%
Smokers	Ex and current 72.3%	Ex and current 70.9%
Diabetics	17.9% (of 510 cases for whom information available)	15.3% (of 510 cases for whom information available)
Hypertension/blood pressure		
Hyperlipidaemia	36%	32.8%
Obesity or weight	23.7%, BMI (mean $\pm$ SD) 26.1 $\pm$ 3.8	19.1%, BMI (mean $\pm$ SD) 25.9 $\pm$ 3.9
Angina		
History of vascular therapy		
Other		
Withdrawals		
Withdrawals/loss to follow-up	24 – baseline data only – excluded from analysis	21 – baseline data only – excluded from analysic (two further not analysed, for PFWD, but HRQoL available)
	16 – lost to follow-up	14 – lost to follow-up
	Nine – did not comply with treatment protocol/had concomitant medication	12 – did not comply with treatment protocol/had concomitant medication
	Four – referral to hospital	Six – referral to hospital
Results		
MWD <i>n</i> in analysis		
MWD baseline		
MWD follow-up		
MWD change		
-		
MWD between-group comparison		
PFWD <i>n</i> in analysis	358	349
PFWD baseline	Mean 389 (SD 389) m	Mean 424 (SD 432) m
PFWD follow-up	Mean 593 (SD 500) m	Mean 476 (SD 476) m
PFWD change	Mean 204 (SD 443) m	Mean 51 (SD 455) m
PFWD between-group comparison	Final absolute value $p$ =0.002 Difference $p$ <0.001	
ABPI <i>n</i> in analysis		
ABPI baseline		
ABPI shange		
ABPI change		
ABPI between-group comparison		
Vascular events <i>n</i> in analysis		
Vascular events follow-up		
Vascular events included		
Vascular events reported	One death from MI	Unclear
Vascular events between-group comparison		

Treatment group	Naftidrofuryl oxalate 200 mg t.i.d.	Placebo
AEs <i>n</i> in analysis	Unclear (states 'whole study population' for deaths, but not clear if withdrawals were followed up for AEs, and presumably those lost to follow-up would not have been included)	Unclear (states 'whole study population' for deaths, but not clear if withdrawals were followed up for AEs, and presumably those lost to follow-up would not have been included)
AEs follow-up	Assume 6 months	
AEs reported	One death	Five deaths
	33 serious (one considered to be in relation to the treatment)	34 serious [two considered to be in relation to the treatment (assume assessor was blinded)]
	11 minor (11 gastrointestinal, five skin reactions)	12 minor (eight gastrointestinal, four skin events)
AEs between-group comparison		
Mortality reported	One also reported in AEs	Five also reported in AEs
Mortality between-group comparison		
HRQoL <i>n</i> in analysis	358	351
HRQoL baseline	Daily living, 65.8 (SD 23.7); pain, 65.6 (SD 18.9); social life, 86.9 (SD 19.8); disease-specific anxiety, 81.1 (SD 20.3); mood, 79.3 (SD 20.1)	Daily living, 66.9 (SD 23); pain, 65 (SD 19.2); social life, 86.1 (SD 20.2); disease-specific anxiety, 80.9 (SD 20.2); mood, 80.7 (SD 18.5)
HRQoL follow-up	Daily living, 73.3 (SD 25); pain, 72 (SD 19.2); social life, 90.0 (SD 16.9); disease-specific anxiety, 83 (SD 20.3); mood, 82.8 (SD 18.5)	Daily living, 65.5 (SD 26.2); Pain, 64.6 (SD 23.1); social life, 84.1 (SD 24.6); disease-specific anxiety, 82 (SD 19.3); mood, 79.5 (SD 22.4)
HRQoL change	(Read from graph/calculated from tables): daily living, 7.5/7.5; pain, 8.4/6.4; social life, 3.1/3.1; disease-specific anxiety, 0.2/1.9; mood, 3.5/3.5	(Read from graph/calculated from tables): daily living,—1.3/—1.4; pain, —0.4/—0.4; social life, —2.4/—2; disease-specific anxiety, 0.2/1.1; mood, —1.3/—1.2
HRQoL between-group comparison	ANCOVA: daily living, $p$ <0.001; pain, $p$ <0.001; social significant; mood, $p$ =0.03	al life, $p$ =0.001; disease-specific anxiety, non-

ANCOVA, analysis of covariance; BMI, body mass index; F, female; M, male.

## Ruckley 1978<sup>68</sup>

## Study details

Publication type Ruckley 1978,<sup>68</sup> short report in peer-reviewed journal

Additional sources of data

Trial design Unclear if RCT or clinical trial

Country UK
Dates of participant recruitment NR

Sources of funding Lipha Pharmaceuticals UK

# Intervention(s) and comparator

Treatment groups Naftidrofuryl oxalate 300 (100 t.i.d.) mg

Comparator Placebo
Run-in phase No
Treatment duration 12 weeks

Outcome(s)

Follow-up Baseline, 2 weeks, 4 weeks, then every 4 weeks until 24 weeks

Outcomes and measures PFWD: not explicit that treadmill was used, but likely that it was. Categorised as < 100 yards = severe,

100-200 yards = moderate, > 200 yards = mild

AEs: patient self-report

Notes on statistics Wilcoxon rank-sum test

Population

Eligibility criteria Consecutive patients attending a peripheral vascular clinic with stable claudication

Concomitant interventions allowed

or excluded

Allowed: all patients asked to take regular exercise

Power calculation NR Nrandomised to treatments 50

included in review

Treatment group	Naftidrofuryl oxalate 100 mg t.i.d.	Placebo
N randomised to treatment		
Baseline characteristics		
Age		
Gender		
Smokers		
Diabetics		
Hypertension/blood pressure		
Hyperlipidaemia		
Obesity or weight		
Angina		
History of vascular therapy		
Other	Severity: 15 mild, three moderate, seven severe	Severity: nine mild, six moderate, 10 severe
Withdrawals		
Withdrawals/loss to follow-up	One patient failed to attend final test, NR which group	
Results		
MWD <i>n</i> in analysis		
MWD baseline	Severity: 15 mild, three moderate, seven severe	Severity: nine mild, six moderate, 10 severe
MWD follow-up		
MWD change		
MWD between-group comparison	Not significant at $p = 0.05$	
PFWD <i>n</i> in analysis		
PFWD baseline		
PFWD follow-up		
PFWD change		
PFWD between-group comparison		
ABPI <i>n</i> in analysis		
ABPI baseline		
ABPI follow-up		
ABPI change		
ABPI between-group comparison		
Vascular events <i>n</i> in analysis		
Vascular events follow-up		
Vascular events included		
Vascular events included  Vascular events reported		
Vascular events between-group comparison		

Treatment group	Naftidrofuryl oxalate 100 mg t.i.d.	Placebo
AEs <i>n</i> in analysis	25	25
AEs follow-up	12 weeks	
AEs reported	Vertigo 8%	Epigastric pain 4%
	Nausea 8%	Indigestion 4%
	Slight insomnia 8%	Constipation 4%
		Headache and nausea 4%
AEs between-group comparison		
Mortality reported		
Mortality between-group comparison		
HRQoL <i>n</i> in analysis		
HRQoL baseline		
HRQoL follow-up		
HRQoL change		
HRQoL between-group compariso		