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Gateways to Clinical Trials

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SUMMARY

Gateways to Clinical Trials is a guide to the most recent clinical trials in current literature and congresses, which has been retrieved from the Clinical Studies knowledge area of Prous Science ***Integrity****, the world's first drug discovery and development portal, providing information on study design, treatments, conclusions and references. This issue focuses on the following selection of drugs: Abacavir sulfate; abciximab; abetimus sodium; adalimumab; aldesleukin; almotriptan; alteplase; amisulpride; amitriptyline hydrochloride; amoxicillin trihydrate; atenolol; atorvastatin calcium; atrasentan; Beclometasone dipropionate; bosentan; Captopril; ceftriaxone sodium; cerivastatin sodium; cetirizine hydrochloride; cisplatin; citalopram hydrobromide; Dalteparin sodium; darusentan; desirudin; digoxin; Efalizumab; enoxaparin sodium; ertapenem sodium; esomeprazole magnesium; estradiol; ezetimibe; Famotidine; farglitazar; fluorouracil; fluticasone propionate; fosamprenavir sodium; Glibenclamide; glucosamine sulfate; Heparin sodium; HSPPC-96; hydrochlorothiazide; Imatinib mesilate; implitapide; Lamivudine; lansoprazole; lisinopril; losartan potassium; l-Propionylcarnitine; Melagatran; metformin hydrochloride; methotrexate; methylsulfinylwarfarin; Nateglinide; norethisterone; Olmesartan medoxomil; omalizumab; omapatrilat; omeprazole; oseltamivir phosphate; oxatomide; Pantoprazole; piperacillin sodium; pravastatin sodium; Quetiapine hydrochloride; Rabeprazole sodium; raloxifene hydrochloride; ramosetron hydrochloride; ranolazine; rasburicase; reboxetine mesilate; recombinant somatropin; repaglinide; reteplase; rosiglitazone; rosiglitazone maleate; rosuvastatin calcium; Sertraline; simvastatin; sumatriptan succinate; Tazobactam sodium; tenecteplase; tibolone; tinidazole; tolterodine tartrate; troglitazone; Uniprost; Warfarin sodium; Ximelagatran.* © 2002 Prous Science. All rights reserved.

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Indications	Design	Treatment	n	Conclusions	Ref.
CARDIAC AND VASCULAR DISORDERS					
Angina pectoris	Randomized Double-blind Multicenter	**Omapatrilat**, 10-80 mg x 3 wk **Placebo**	348	Omapatrilat was effective as anti-ischemic and antianginal treatment in stable effort-induced angina pectoris	1
Angina pectoris	Randomized Double-blind Crossover	**Ranolazine**, 500 mg b.i.d. x 7 d **Ranolazine**, 1000 mg b.i.d. x 7 d **Ranolazine**, 1500 mg b.i.d. x 7 d **Placebo**	191	Ranolazine could be useful in angina	2
Atrial fibrillation, Embolic stroke	Randomized Open	**Ximelagntran**, 36 mg p.o. b.i.d. x 21-24 months **Warfarin**, (INR of 2-3) x 21-24 months	254	Ximelagatran was effective and well tolerated for the prevention of stroke and systemic embolism with no need for routine coagulation monitoring	3
Heart failure	Randomized Double-blind Multicenter	**Omapatrilat**, 1 mg p.o. (n = 11) **Omapatrilat**, 2.5 mg p.o. (n = 13) **Omapatrilat**, 5 mg p.o. (n = 12) **Omapatrilat**, 10 mg p.o. (n = 15) **Omapatrilat**, 25 mg p.o. (n = 15) **Omapatrilat**, 50 mg p.o. (n = 14) **Placebo** (n = 33)	151	Omapatrilat induced dose-related improvements in hemodynamic parameters in patients with heart failure. It induced dose-related reductions in pulmonary capillary wedge pressure, mean arterial pressure and systemic vascular resistance and increases in atrial natriuretic peptide and cGMP levels	4
Heart failure	Randomized Double-blind Multicenter	**Omapatrilat**, 10 → 40 mg p.o. o.d. x 12 wks **Lisinopril**, 5 → 20 mg p.o. o.d. x 12 wks	573	Health perception measured by a Visual Analogue Scale and NYHA was a better predictor of clinical events than treadmill exercise time in patients with heart failure treated with omapatrilat or lisinopril (IMPRESS trial)	5
Heart failure	Randomized Double-blind Multicenter	**Darusentan**, 30 mg p.o. **Darusentan**, 100 mg p.o. **Darusentan**, 300 mg p.o. **Placebo**	157	Long-term treatment with darusentan improved hemodynamics without neurohormonal activation or impairment of renal function in patients with congestive heart failure	6
Heart failure, dilated cardiomyopathy	Randomized Double-blind	**Recombinant somatropin**, 2 IU s.c. o.d x 14 wks **Placebo**	50	Recombinant somatropin induced an increase of insulin-like growth factor-1 of more than77 µg/l and caused significant improvement of ejection fraction in patients with heart failure. Serum levels of insulin-like growth factor-1 reflecting growth hormone secretion were inversely proportional to the severity of heart failure in patients with dilated cardiomyopathy	7
Myocardial infarction	Open Multicenter	**Reteplase + Abciximab** (n = 20) **Reteplase** (n = 18) **Alteplase** (n = 20) **Tenecteplase** (n = 10)	68	Alteplase and reteplase produced remarkable FXIIa activation and systemic plasminemia whereas abciximab and tenecteplase caused insignificant activation of the factor XII system in acute myocardial infarction	8
Myocardial infarction	Open Multicenter	**Tenecteplase**, 30-50 mg + **Enoxaparin**, 30 mg i.v. bolus → **Enoxaparin**, 1mg/kg s.c. o.d. x 7 d (n = 2040) **Tenecteplase**, 15-25 mg + **Abciximab**, 0.25 mg/kg i.v. bolus + **Heparin**, 40 U/kg i.v. bolus → **Abciximab**, 0.125 µg/kg i.v.over 12 h + **Heparin**, 7 U/kg/h i.v. over 48 h [to aPTT 50-70 s] (n = 2017) **Tenecteplase**, 30-50 mg + **Heparin**, 60 U/kg i.v. bolus → **Heparin**, 12 U/kg/h i.v. over 48 h [to aPTT 50-70 s] (n = 2038)	6095	Tenecteplase plus enoxaparin was more safe and effective than tenecteplase plus unfractionated heparin or tenecteplase plus abciximab and unfractionated heparin in acute myocardial infarction (The ASSENT-3 trial)	9

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Indications	Design	Treatment	n	Conclusions	Ref.
Essential hypertension	Randomized Double-blind Multicenter	**Olmesartan**, 10-20 mg p.o. o.d.+ **Hydrochlorothiazide**, 25 mg p.o. o.d. x 12 wks (n = 164) **Atenolol**, 50-100 mg p.o. o.d. + **Hydrochlorothiazide**, 25 mg p.o. o.d. x 12 wks (n = 164)	328	Olmesartan and atenolol were equally effective when added to hydrochlorothiazide for the treatment of moderate to severe hypertension	10
Essential hypertension	Randomized Double-blind Multicenter	**Olmesartan**, 10-20 mg p.o. o.d. x 24 wks + **Hydrochlorothiazide**, 12.5-25 mg p.o. o.d. (n = 160) **Losartan**, 50-100 mg p.o. o.d. x 24 wks + **Hydrochlorothiazide**, 12.5-25 mg p.o. o.d. (n = 156)	316	Olmesartan demonstrated a blood pressure lowering effect superior to losartan in patients with mild to moderate hypertension	11
Essential hypertension	Randomized Double-blind Multicenter	**Olmesartan**, 10-20 mg p.o. o.d. x 12 wks (n = 165) **Atenolol**, 50-100 mg p.o. o.d. x 12 wks (n = 161)	326	Olmesartan and atenolol demonstrated the same efficacy in reducing diastolic blood pressure but olmesartan was more effective than atenolol in reducing systolic blood pressure in patients with mild to moderate hypertension	12
Essential hypertension	Randomized Double-blind Multicenter	**Olmesartan**, 5-20 mg p.o. o.d. x 12 wks (n = 148) **Captopril**, 12.5-50 mg p.o. b.i.d. x 12 wks (n = 143)	291	Olmesartan demonstrated a superior blood pressure lowering effect to captopril in patients with mild to moderate hypertension	13
Essential hypertension	Open	**Olmesartan**, 5-40 mg p.o. o.d. x 52 wks	26	Olmesartan was safe and effective in the long-term treatment of hypertension by decreasing angiotensin I and II levels	14
Hypertension and nephropathy in diabetes mellitus non insulin-dependent	Randomized Double-blind Multicenter	**Losartan**, 50 mg p.o. o.d. x 3.4 year (n = 751) **Placebo** (n = 762)	1513	Losartan improved renal outcomes in patients with type 2 diabetes and was well tolerated	15
Hypertension in diabetes mellitus non insulin-dependent	Randomized Double-blind	**Rosiglitazone**, 4 mg p.o. b.i.d. x 12 wks (n = 9) **Placebo** (n = 9)	18	Rosiglitazone improved insulin sensitivity and reduced both systolic and diastolic ambulatory blood pressure in patients with impaired glucose tolerance	16
Diabetes mellitus non insulin dependent and microalbuminuria	Randomized Double-blind Open Multicenter Pooled data	Study I: **Rosiglitazone**, 4 mg/d p.o. x 26 wks (n = 166) **Rosiglitazone**, 8 mg/d p.o. x 26 wks (n = 169) **Placebo** (n = 158) Study II: **Rosiglitazone**, 8 mg/d p.o. x 52 wks (n = 104) **Glibenclamide**, 10.5 mg/d p.o. x 52 wks (n = 99)		Rosiglitazone reduced albumin excretion more than glibenclamide or placebo, correlating with changes in mean arterial blood pressure (systolic and diastolic). The beneficial effects of rosiglitazone on microalbuminuria and markers of vascular and endothelial integrity suggested that rosiglitazone improved vascular function, resulting in reduced blood pressure and urinary albumin excretion. Rosiglitazone had a potentially beneficial effect on the prevention of renal and vascular complications in type 2 diabetes	17
Cardiovascular disorders in diabetes mellitus non insulin-dependent		Study I: **Rosiglitazone**, 4 mg o.d. x 52 wks (n = 152) **Rosiglitazone**, 8 mg o.d. x 52 wks (n = 146) **Glibenclamide** x 52 wks (n = 158) Study II: **Rosiglitazone**, 2 mg o.d. + **Sulfonylurea** x 26 wks (n = 198) **Rosiglitazone**, 4 mg o.d. + **Sulfonylurea** x 26 wks (n=183) **Sulfonylurea** x 26 wks (n = 192) Study III: **Rosiglitazone**, 4 mg o.d. + **Metformin** x 26 wks (n=115) **Rosiglitazone**, 8 mg o.d. + **Metformin** x 26 wks (n=109) **Metformin** x 26 wks (n = 113)	1208	The rosiglitazone-mediated decrease in insulin resistance could reduce cardiovascular disease risk	18

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GATEWAYS TO CLINICAL TRIALS

Indications	Design	Treatment	n	Conclusions	Ref.
Periphera vascular disease and hyper-cholesterolemia	Randomized Double-blind	**Pravastatin**, 40 mg/d p.o. x 4 month (n = 17) **Placebo** (n = 15)	32	Pravastatin induced cholesterol reduction and improved endothelial function and reduced inflammation in patients with peripheral arterial insufficiency	19
Intermittent claudication	Randomized Double-blind Multicenter	**L-Propionylcarnitine**, 1 g p.o. b.i.d. x 6 months (n = 85) **Placebo** (n = 76)	161	L-Propionylcarnitine was effective in improving treadmill exercise performance and functional status in patients with peripheral arterial disease and claudication	20
Pulmonary hypertension	Open Multicenter	**Uniprost**, 16 ng/kg/min s.c. x 6 months (n = 156) **Uniprost**, 25 ng/kg/min s.c. x 12 months (n = 102) **Uniprost**, 24 ng/kg/min s.c. x 15 months (n = 63) **Uniprost**, 31 ng/kg/min s.c. x 18 months (n = 46) **Uniprust**, 38 ng/kg/min s.c. x 21 months (n = 15)	631	Long-term treatment with uniprost improves exercise in patients with pulmonary hypertension	21
Pulmonary hypertension primary or secondary to Scleroderma, Systemic lupus erythematosus	Randomized Double-blind Multicenter	**Bosentan** 62.5 → 125 mg b.i.d. x 16 wks **Bosentan** 62.5 → 250 mg b.i.d. x 16 wks **Placebo**	213	Bosentan (125 mg b.i.d.) improved exercise capacity and reduced the risk of clinical worsening in patients with pulmonary hypertension with good tolerability (The BREATHE-1 trial)	22
Pulmonary embolism	Open	**Ximelagatran**, 48 mg p.o. b.i.d. x 6-9 d + **Heparin** or **Warfarin**	12	Ximelagatran was effective and well tolerated in the treatment of hemodynamically stable pulmonary embolism at fixed doses (The THRIVE-IV trial)	23
Venous thrombosis	Randomized Double-blind Multicenter	**Ximelagatran**, 24 mg p.o. b.i.d. x 2 wks **Ximelagatran**, 36 mg p.o. b.i.d. x 2 wks **Ximelagatran**, 48 mg p.o. b.i.d. x 2 wks **Ximelagatran**, 60 mg p.o. b.i.d. x 2 wks **Dalteparin** → **Warfarin**	350	Ximelagatran was effective as anticoagulant therapy in the progression of acute deep venous thrombosis (The THRIVE-I trial)	24
Deep venous thrombosis prophylaxis in artluroplasty	Randomized Double-blind Multicenter	**Melagatran**, 3 mg s.c. → **Ximelagatran**, 24 mg p.o. b.i.d. x 8-11 d **Enoxaparin**, 40 mg s.c. o.d. x 8-11 d	2788	Postoperative administration of subcutaneous melagatran followed by oral ximelagatran was found to be as safe and effective as enoxaparin as prophylaxis against venous thromboembolism. The time interval between surgery and first dose may be important in order to ensure optimal efficacy	25
Healthy Volunteers	Randomized Double-blind Crossover	**Warfarin**, x 13 d → **Olmesartan**, 40 mg p.o. o.d. x 7 d **Warfarin**, x 13 d → **Placebo** x 7 d	24	The coadministration of olmesartan and warfarin did not alter coagulation factors and was well tolerated	26
Healthy Volunteers	Randomized Open	**Xinelagatran**, 20 mg p.o. **Ximelagatran**, 40 mg p.o. **Ximelagatran**, 80 mg p.o. **Desirudin**, 0.4 mg/kg i.v. bolus → 0.15 mg/kg/h x 2 h → 0.075 mg/kg/h x 3 h	60	A dose-dependent reduction in *ex-vivo* thrombus formation under low and high shear rate conditions was noted with ximelagatran	27
Healthy Volunteers	Open	**Omapatrilat**, 40 mg p.o. s.d.	48	The effects of omapatrilat on blood pressure did not depend on the age or gender of the patients	28
Healthy Volunteers	Randomized Double-blind	**Pravastatin**, 40 mg/d x 6 month (n = 24) **Placebo** (n = 26)	50	Pravastatin decreased serum matrix metalloproteinase levels in healthy men independently of changes in lipid levels. This could reflect a reduction in nonsymptomatic chronic arterial inflammation	29

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Indications	Design	Treatment	n	Conclusions	Ref.
Healthy Volunteers	Randomized Double-blind Crossover	**Digoxin**, 0.375 mg p.o. o.d. x 10 d → + **Olmesartan**, 20 mg p.o. o.d. x 7 d **Digoxin**, 0.375 mg p.o. o.d. x 10 d → + **Placebo** x 7 d	24	The coadministration of olmesartan and digoxin was safe	30
GASTROINTESTINAL DISORDERS					
Gastrointestinal carcinoma	Open Multicenter	**Cisplatin**, 20 mg/m² i.v. infusion over 1 h before radiotherapy 2x/wk + **Fluorouracil**, 300 mg/m²/d i.v. continuous infusion x 5x/wk + **Radiation** 1.5 Gy/fraction 5x/wk + Hyperthermia 42.5 – 44.0 °C 2x/wk + **Ramosetron**, 0.3 mg i.v. x 5x/wk x 3 wks	15	Ramosetron was useful for the treatment of nausea and vomiting induced by chemotherapy for the treatment of solid tumors	31
Gastroenteritis helicobacter	Randomized	**Famotidine**, 40 mg b.i.d. + **Amoxicillin**, 1 g b.i.d. + **Tinidazole**, 500 mg b.i.d. x 2 wks (n = 60) **Omeprazole**, 20 mg b.i.d. + **Amoxicillin**, 1 g b.i.d. + **Tinidazole**, 500 mg b.i.d. x 2 wks (n = 60)	120	Famotidine and omeprazole administered together with amoxicillin and tinidazole showed similar rates of *H. pylori* eradication	32
Gastroesophageal reflux disease	Randomized Double-blind Multicenter	**Omeprazole**, 10 mg p.o. o.d., x 7 d (n = 23) **Rabeprazole**, 10 mg p.o. b.i.d. x 7 d (n = 24) **Rabeprazole**, 20 mg p.o. o.d. x 7 d (n = 22) **Placebo** (n = 23)	92	Rabeprazole 10 mg b.i.d. and 20 mg o.d. showed similar efficacy compared to omeprazole 20 mg o.d. in decreasing esophageal acid exposure	33
Gastroesophageal reflux disease	Randomized Open Multicenter	**Pantoprazole**, 20 mg p.o. o.d. x 4 wks (n = 166) **Omeprazole**, 20 mg p.o. o.d. x 4 wks (n = 161)	328	Pantoprazole showed efficacy similar to omeprazole in symptom relief and healing in patients with gastroesophageal reflux disease	34
Gastroesophageal reflux disease	Randomized Open Crossover	**Esomeprazole**, 40 mg p.o. o.d. x 5 d **Rabeprazole**, 20 mg p.o. o.d. x 5 d	35	Esomeprazole 40 mg provided significantly faster and more effective acid control than rabeprazole 20 mg	35
Gastro-oesophageal reflux disease	Randomized Double-blind Multicenter	**Esomeprazole**, 40 mg p.o. o.d. x 8 wks **Lansoprazole**, 30 mg p.o. o.d. x 8 wks	5241	Esomeprazole 40 mg was more effective than lansoprazole 30 mg for the healing of erosive esophagitis	36
Healthy Volunteers	Randomized Open Crossover	**Esomeprazole**, 40 mg p.o. **Lansoprazole**, 30 mg p.o.	28	Esomeprazole 40 mg was more effective than lansoprazole 30 mg after single dosing	37
Healthy Volunteers	Randomized Open Crossover	Study I: (n = 12) **Omeprazole**, 20 mg p.o. o.d. x 7 d **Lansoprazole**, 30 mg p.o. o.d. x 7 d Study II: (n = 24) **Omeprazole**, 40 mg p.o. o.d. x 7 d **Lansoprazole**, 30 mg p.o. o.d. x 7 d	36	Omeprazole 40 mg increased the intragastric pH for a longer duration than lansoprazole	38
IMMUNE SYSTEM DISORDERS					
Conjunctivitis and allergic rhinitis	Randomized Double-blind Multicenter	**Omalizumab**, 150-300 mg 1x/4 wks or 225-375 mg/kg/IgE IU/ml 1x/2wk s.c. x 24 wks + Specific immmunotherapy (ALK-Abello) for birch/grass pollen **Placebo** + Specific immmunotherapy (ALK-Abello) for birch/grass pollen	225	Omalizumab was safe and effective in birch and grass pollen-induced seasonal allergic rhinoconjuntivitis	39
Conjunctivitis and allergic rhinitis	Randomized Multicenter	**Omalizumab**, s.c. + Specific immmunotherapy for birch pollen (n = 22) **Omalizumab**, s.c. + Specific immmunotherapy for grass pollen (n = 23) **Placebo** + Specific immmunotherapy for birch pollen (n = 22) **Placebo** + Specific immmunotherapy for grass pollen (n = 24)	91	Omalizumab was effective in reducing *in vitro* sulfido-leukotriene release to birch and grass pollen in children and adolescents with seasonal allergic rhinoconjuntivitis	40
Allergic rhinitis	Randomized Double-blind Multicenter	**Omalizumab**, 0.016 mg/kg/IgE IU/ml s.c. 1x/2-4 wks x 16 wks (n = 144) **Placebo** (n = 145)	289	Omalizumab was well tolerated and effective in perennial allergic rhinitis	41

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