

# Clinical trials of nesiritide

TrialResults-center [www.trialresultscenter.org](http://www.trialresultscenter.org)

## 1 heart failure

Trial	Treatments	Patients	Trials design and methods
<b>nesiritide vs control</b>			
<b>NSGET (comparative trial) , 2000</b> n=203/102 follow-up: <5 days	nesiritide(0.015 and 0.030 microg/kg/min versus usual care	acutely decompensated heart failure requiring invasive monitoring	Parallel groups open US
<b>nesiritide vs placebo</b>			
<b>ASCEND-HF , 2011</b> <i>unpublished</i> [NCT00475852] n=3496/3511 follow-up: 30 days	intravenous nesiritide for 24 hours to 7 days on top of standard therapy versus matching placebo	Patients hospitalized for heart failure (within 24 hours of hospitalization and institution of acute IV therapy for ADHF)	Parallel groups double-blind North America, Europe, Latin America, Asia-Pacific region
<b>BNP-CARDS , 2007</b> [NCT00186329] n=39/36 follow-up: 7 days	nesiritide as a 0.01-g/kg/min infusion for 48 hours versus placebo	acute decompensated heart failure with moderate to severe renal insufficiency	Parallel groups Double blind US
<b>FUSION 2 , 2008</b> [NCT00091520] n=911 follow-up: 12 weeks	nesiritide (2 g/kg bolus plus 0.01 g/kg-per-minute infusion for four to six hours) versus placebo	patients with ACC/AHA stage C/D heart failure with two recent heart-failure hospitalizations, an ejection fraction of less than 40% , and NYHA class 4 symptoms or NYHA class 3 symptoms with creatinine clearance less than 60 mL/min	Parallel groups double-blind
<b>NSGET (efficacy trial) , 2000</b> n=85/42 follow-up:	nesiritide(0.015 and 0.030 microg/kg/min versus placebo	acutely decompensated heart failure requiring invasive monitoring	
<b>PROACTION , 2003</b> n=127/123 follow-up: 30 days	nesiritidefor at least 12h versus placebo	patients presenting to the ED with acutely decompensated HF and dyspnea at rest or with minimal activity	Parallel groups double-blind USA

continued...

Trial	Treatments	Patients	Trials design and methods
<b>VMAC (intravenous nesiritide) , 2002</b> [NCT00083772] n=204/142 follow-up:	intravenous nesiritidefor 3 hours versus placebo	acutely decompensated heart failure requiring hospitalization	double-blind USA
<b>nesiritide vs dobutamine</b>			
<b>PRECEDENT , 2002</b> [NCT00270400] n=NA follow-up:	nesiritide(0.015 or 0.03 microg/kg/min) versus Dobutamine (>or =5 microg/kg/min)	Symptomatic, Decompensated CHF	Parallel groups open
<b>nesiritide vs nitroglycerin</b>			
<b>VMAC (24h) , 2002</b> [NCT00083772] n=280/218 follow-up:	nesiritideinfusion for 24 hours versus nitroglycerin	acutely decompensated heart failure requiring hospitalization	
<b>nesiritide vs standard care</b>			
<b>FUSION 1 , 2004</b> [NCT00270361] n=NA follow-up: 12 weeks	nesiritide 0.005 microg/kg/min or 0.010 microg/kg/min once weekly versus standard care	outpatient with co-morbid advanced heart failure and renal insufficiency	Parallel groups open

More details and results :

- vasodilators therapy for heart failure in all type of patient at <http://www.trialresultscenter.org/go-Q79>
- vasodilators therapy for heart failure in acute decompensated heart failure at <http://www.trialresultscenter.org/go-Q472>

## References

### NSGET (comparative trial), 2000:

Colucci WS, Elkayam U, Horton DP, Abraham WT, Bourge RC, Johnson AD, Wagoner LE, Givertz MM, Liang CS, Neibaur M, Haught WH, LeJemtel TH N Engl J Med 2000 Jul 27;343:246-53 [10911006]

### ASCEND-HF, 2011:

unpublished

Burnett JC Jr, Korinek J The tumultuous journey of nesiritide: past, present, and future. Circ Heart Fail 2008 May;1:6-8 [19808264] [10.1161/CIRCHEARTFAILURE.108.776294](https://doi.org/10.1161/CIRCHEARTFAILURE.108.776294)

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O'Connor CM, Starling RC, Hernandez AF, Armstrong PW, Dickstein K, Hasselblad V, Heizer GM, Komajda M, Massie BM, McMurray JJ, Nieminen MS, Reist CJ, Rouleau JL, Swedberg K, Adams KF Jr, Anker SD, Atar D, Battler A, Botero R, Bohidar NR, Butler J, Clausel Effect of nesiritide in patients with acute decompensated heart failure. *N Engl J Med* 2011 Jul 7;365:32-43 [[21732835](#)] [10.1056/NEJMoa1100171](#)

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#### **FUSION 2, 2008:**

Yancy CW, Krum H, Massie BM, Silver MA, Stevenson LW, Cheng M, Kim SS, Evans R The Second Follow-up Serial Infusions of Nesiritide (FUSION II) trial for advanced heart failure: study rationale and design. *Am Heart J* 2007;153:478-84 [[17383282](#)]

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#### **VMAC (intravenous nesiritide), 2002:**

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## 2 acute heart failure

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More details and results :

- new drug under development for acute heart failure in all type of patients at <http://www.trialresultscenter.org/go-Q640>
- endothelin receptor antagonist for acute heart failure in all type of patients at <http://www.trialresultscenter.org/go-Q643>
- atrial natriuretic peptide for acute heart failure in all type of patients at <http://www.trialresultscenter.org/go-Q644>

## References

### NSGET (comparative trial), 2000:

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Entry terms: Brain Natriuretic Peptide, BNP-32, BNP 32, Nesiritide, B-Type Natriuretic Peptide, BNP Gene Product, Type-B Natriuretic Peptide, Type B Natriuretic Peptide, Natriuretic Peptide Type-B, Natriuretic Peptide Type B, Natriuretic Factor-32, Natriuretic Factor 32, Brain Natriuretic Peptide-32, Brain Natriuretic Peptide 32, Natrecor,