

**STATISTICAL REVIEW AND EVALUATION  
(ADDENDUM #2)**

NDA #: 20-920 Major Amendment

Applicant: Scios Inc.

Drug Name: Natrecor (nesiritide)

Indication: decompensated congestive heart failure

This addendum reports the results of 3-hour dyspnea in catheterized patients and non-catheterized patients, requested by Dr. Throckmorton. The 3-hour dyspnea results observed in the study (Table 4 of statistical review, dated 04/18/01) appeared to be mainly driven by the results of the catheterized patients (Table 4B-1). In the non-catheterized patients, the Natrecor group seemed to have little advantage over the placebo group (Table 4B-2).

Table 4B-1. Catheterized Subject's 3-hour dyspnea evaluation (as randomized)

	Nitroglycerin (N=60)	Natrecor (N=124)	Placebo (N=62)
# of subjects analyzed	60	123	62
Mean $\pm$ se	1.1 $\pm$ 1.3	1.3 $\pm$ 1.1	0.9 $\pm$ 1.2
p-value <sup>1</sup> for comparison to placebo	0.43	0.052	----
p-value <sup>1</sup> for Natrecor vs. NTG		0.31	
Markedly better	8 (13%)	18 (15%)	9 (15%)
Moderately better	17 (28%)	33 (27%)	8 (13%)
Minimally better	14 (23%)	40 (33%)	18 (29%)
No change	16 (27%)	28 (23%)	23 (37%)
Minimally worse	4 ( 7%)	4 ( 3%)	4 ( 6%)
Moderately worse	0 ( 0%)	0 ( 0%)	0 ( 0%)
Markedly worse	1 ( 2%)	0 ( 0%)	0 ( 0%)
p-value <sup>2</sup> for comparison to placebo	0.31	0.030	----
p-value <sup>2</sup> for Natrecor vs. NTG		0.44	

Reviewer's analysis

Table 4B-2. Non-Catheterized Subject's 3-hour dyspnea evaluation (as randomized)

	Nitroglycerin (N=83)	Natrecor (N=80)	Placebo (N=80)
# of subjects analyzed	83	80	80
Mean $\pm$ se	1.4 $\pm$ 1.0	1.4 $\pm$ 1.1	1.3 $\pm$ 1.2
p-value <sup>1</sup> for comparison to placebo	0.47	0.47	----
p-value <sup>1</sup> for Natrecor vs. NTG		0.99	
Markedly better	9 (11%)	16 (20%)	16 (20%)
Moderately better	33 (40%)	21 (26%)	16 (20%)
Minimally better	23 (28%)	24 (30%)	23 (29%)
No change	17 (20%)	17 (21%)	23 (29%)
Minimally worse	1 ( 1%)	1 ( 1%)	2 ( 3%)
Moderately worse	0 ( 0%)	1 ( 1%)	0 ( 0%)
Markedly worse	0 ( 0%)	0 ( 0%)	0 ( 0%)
p-value <sup>2</sup> for comparison to placebo	0.40	0.41	----
p-value <sup>2</sup> for Natrecor vs. NTG		0.96	

Reviewer's analysis

The correlation between 3-hour change in PCWP and 3-hour dyspnea score is 0.21 (nominal p = 0.0009) in the entire catheterized patients, 0.26 (nominal p=0.0046) in the Natrecor group, 0.08 (nominal p=0.57) in the nitroglycerin group, 0.14 (nominal p=0.27) in the placebo group.

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Acting Team Leader

This review consists of 2 pages of text.

cc: NDA 20-920 Major Amendment (Addendum #2)  
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JHung/594-5436/DB1/Natrec2.doc/04-23-2001

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/s/

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4/23/01 04:39:28 PM  
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Need sign-off by 4/24

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