Figures

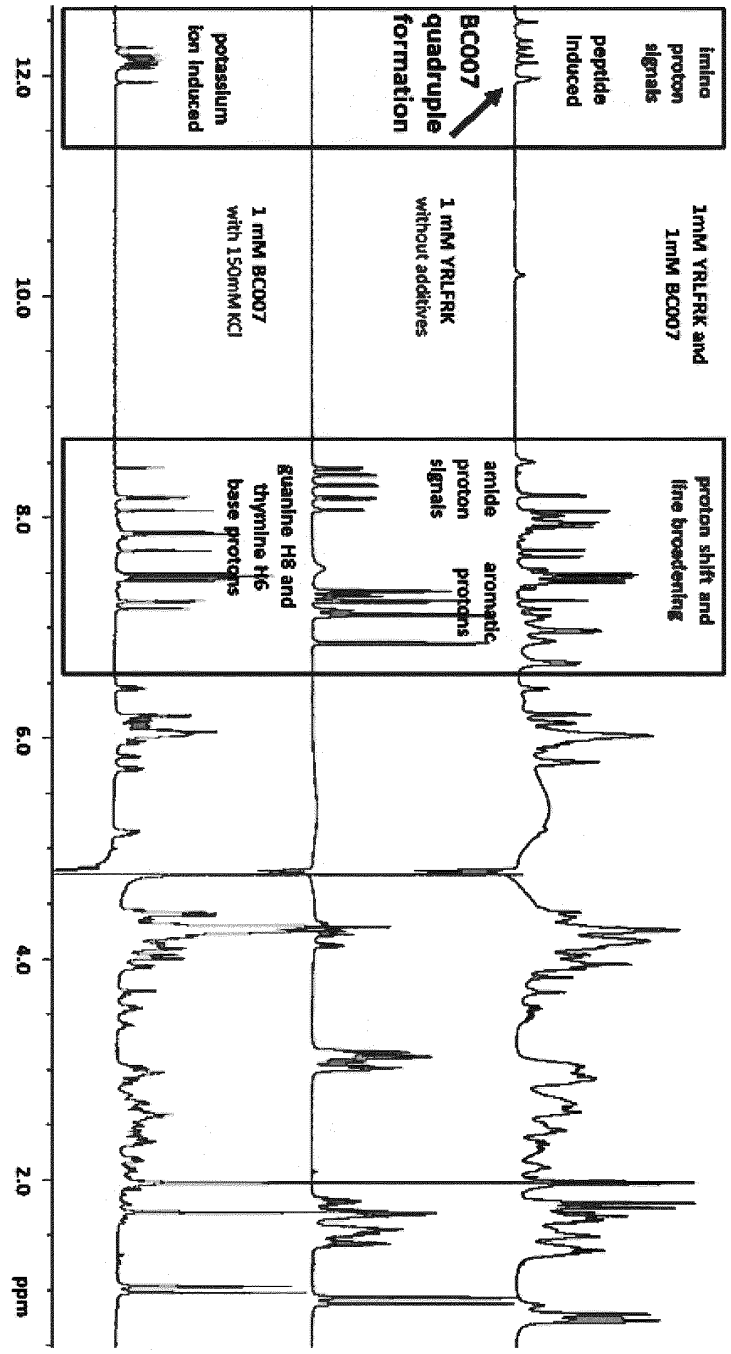


Figure 1

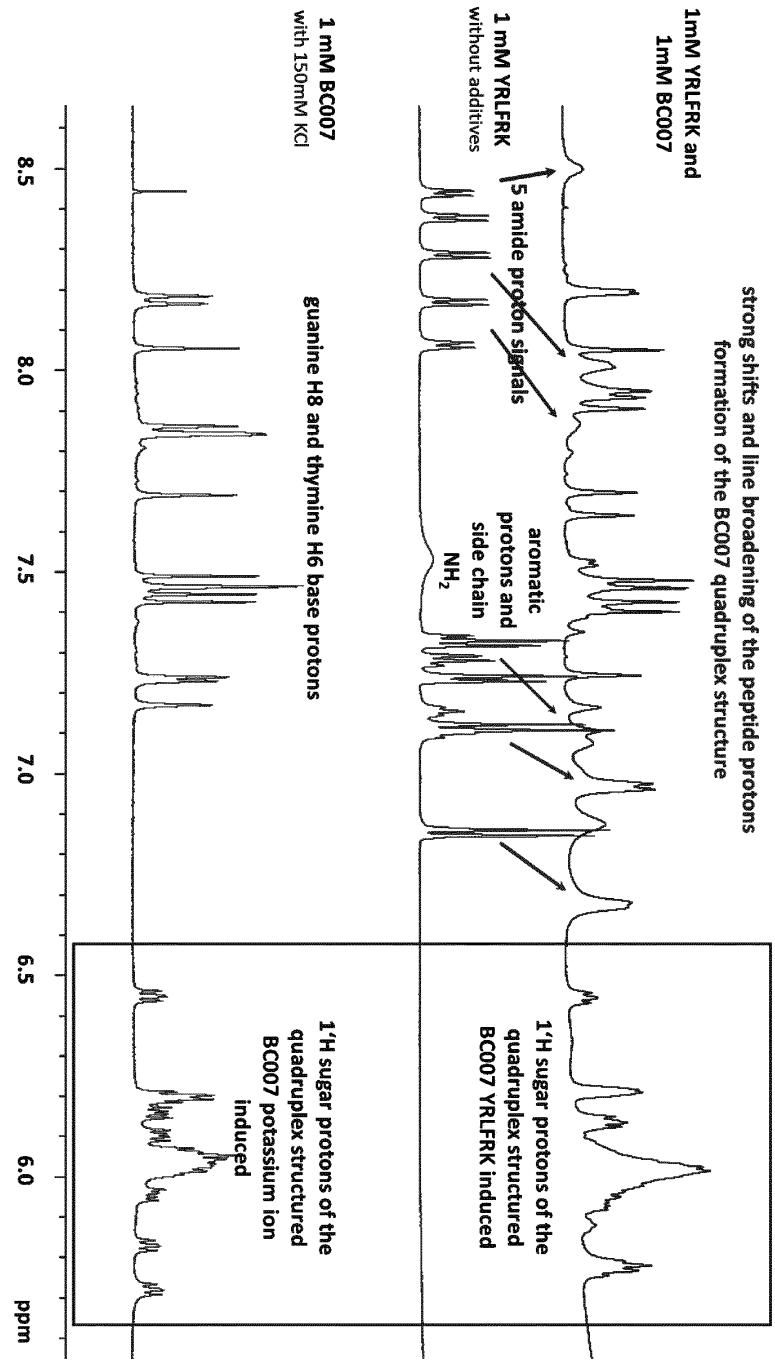

1mM YRLFRK and
1mM BC007
strong shifts and line broadening of the peptide protons
formation of the BC007 quadruplex structure
1 mM YRLFRK
without additives
5 amide proton signals
aromatic
protons and
side chain
NH2
1 mM BC007
with 150mM KCl
guanine H8 and thymine H6 base protons
1'H sugar protons of the
quadruplex structured
BC007 YRLFRK induced
1'H sugar protons of the
quadruplex structured
BC007 potassium ion
induced
8.5
8.0
7.5
7.0
6.5
6.0
ppm

Figure 2

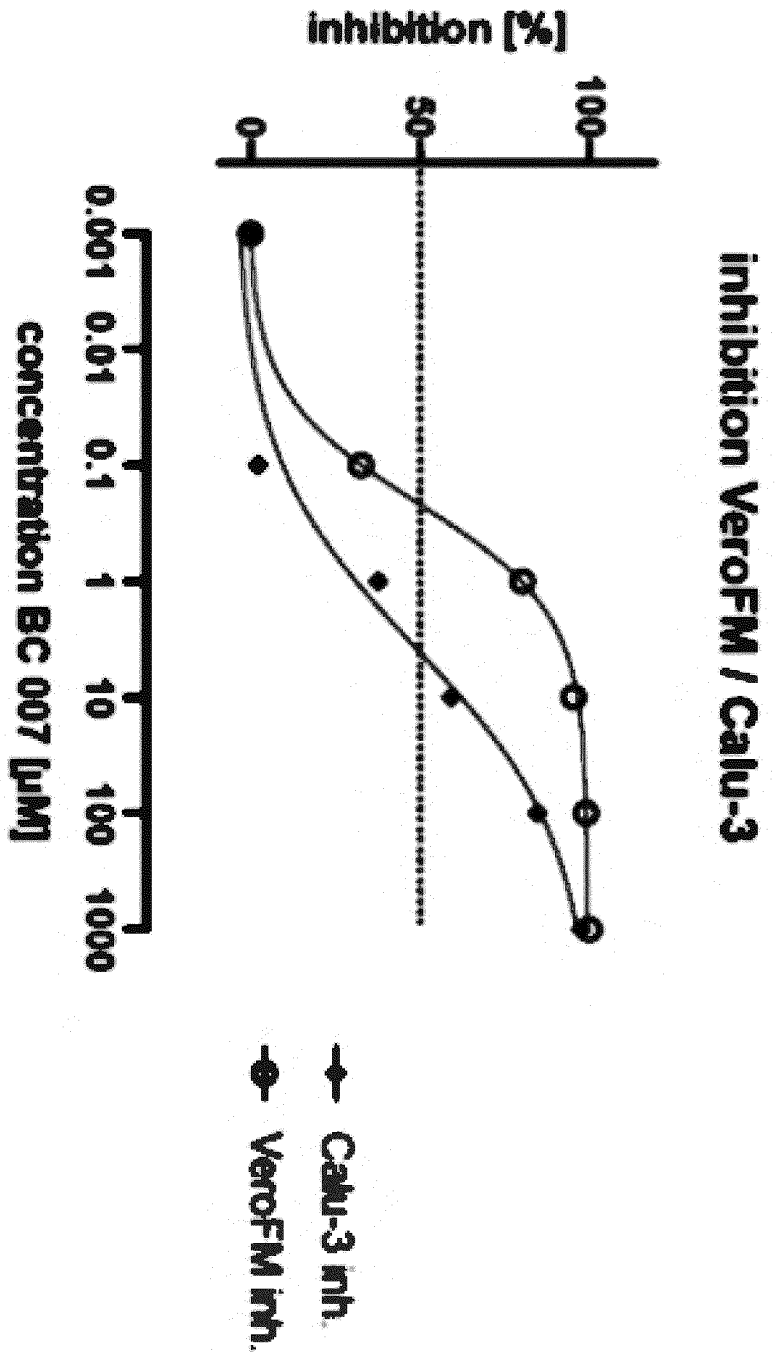

inhibition [%]
0
50
100
inhibition VeroFM / Calu-3
0.001
0.01
0.1
1
10
100
1000
concentration BC 007 [µM]
Calu-3 inh.
VeroFM inh.

Figure 3

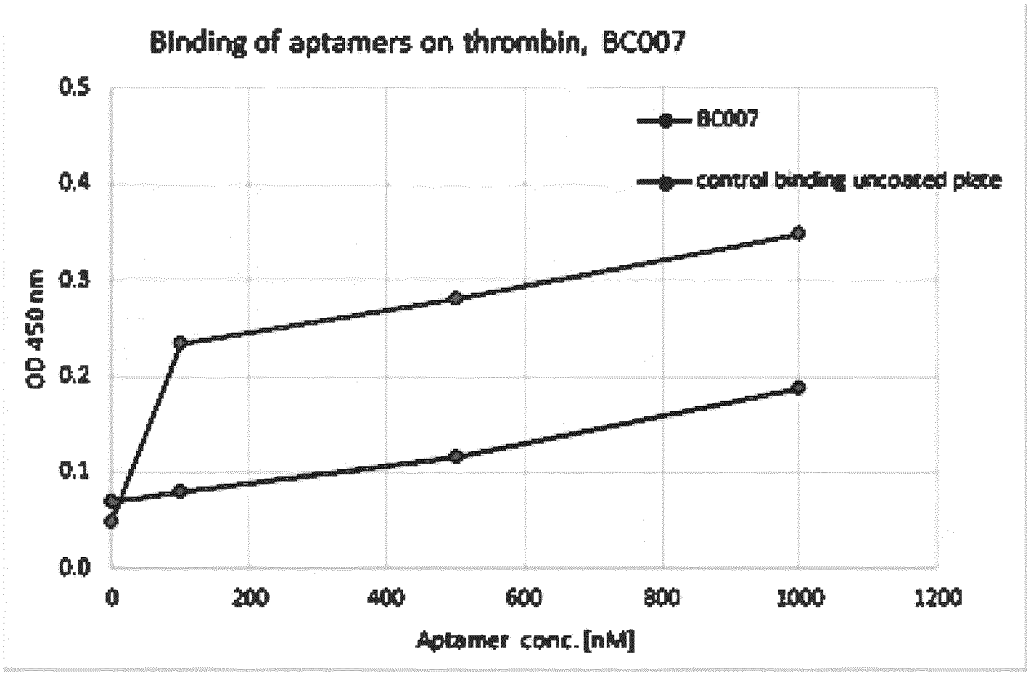
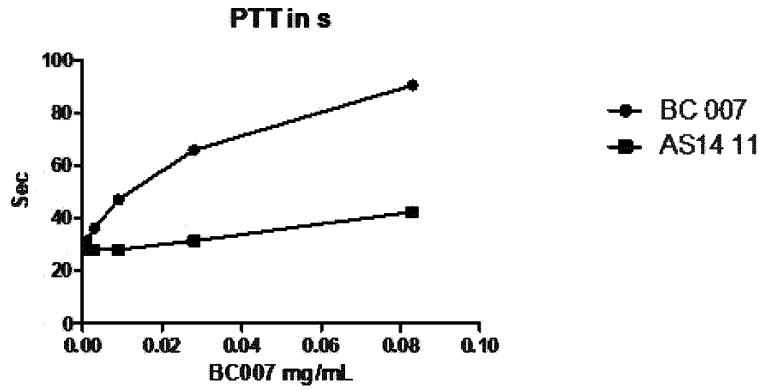

Binding of aptamers on thrombin, BC007
BC007
control binding uncoated place
OD 450 nm
0.5
0.4
0.3
0.2
0.1
0.0
0
200
400
600
800
1000
1200
Aptamer conc. [nM]

Figure 4

A


PTT in s
100
80
60
40
20
0
Sec
0.00
0.02
0.04
0.06
0.08
0.10
BC007 mg/mL
BC 007
AS14 11

B

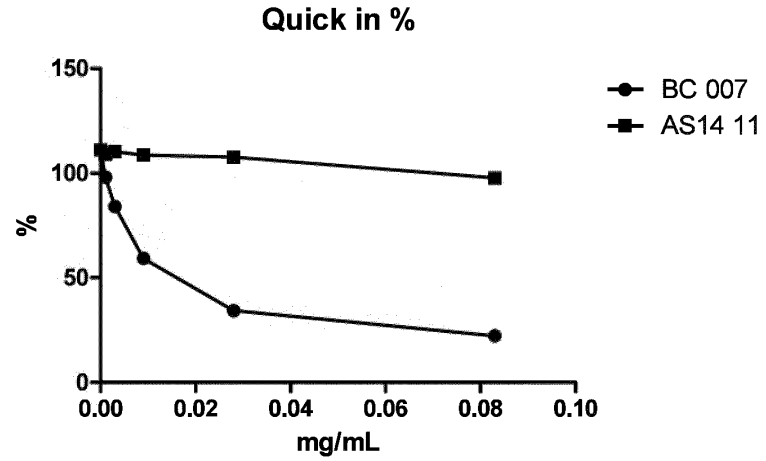

Quick in %
150
100
50
0
%
0.00
0.02
0.04
0.06
0.08
0.10
mg/mL
BC 007
AS14 11

Figure 5

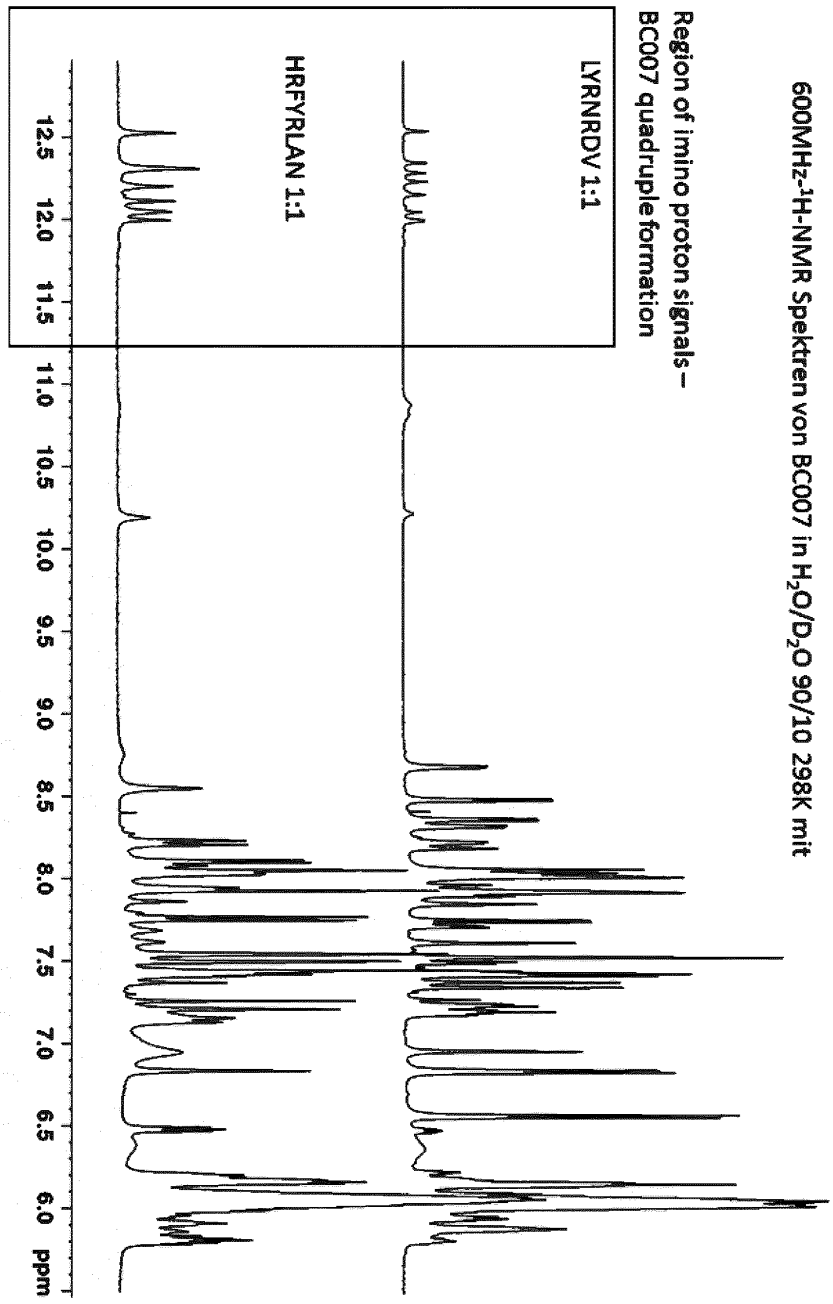

600MHz-¹H-NMR Spektren von BC007 in H2O/D2O 90/10 298K mit
Region of imino proton signals –
BC007 quadruple formation
LYRNRDV 1:1
HRFYRLAN 1:1
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
ppm

Figure 6

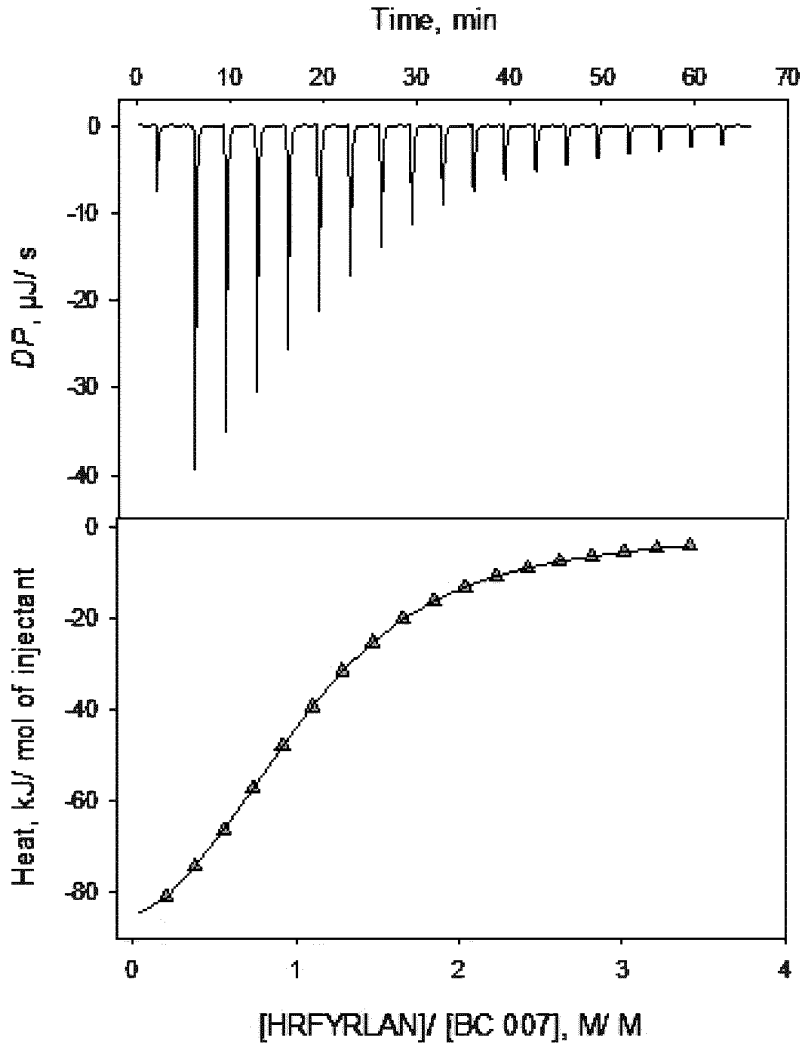

Time, min
0
10
20
30
40
50
60
70
0
-10
-20
-30
-40
DP, µJ/ s
0
-20
-40
-60
-80
Heat, kJ/ mol of injectant
0
1
2
3
4
[HRFYRLAN]/ [BC 007], M/ M

Figure 7

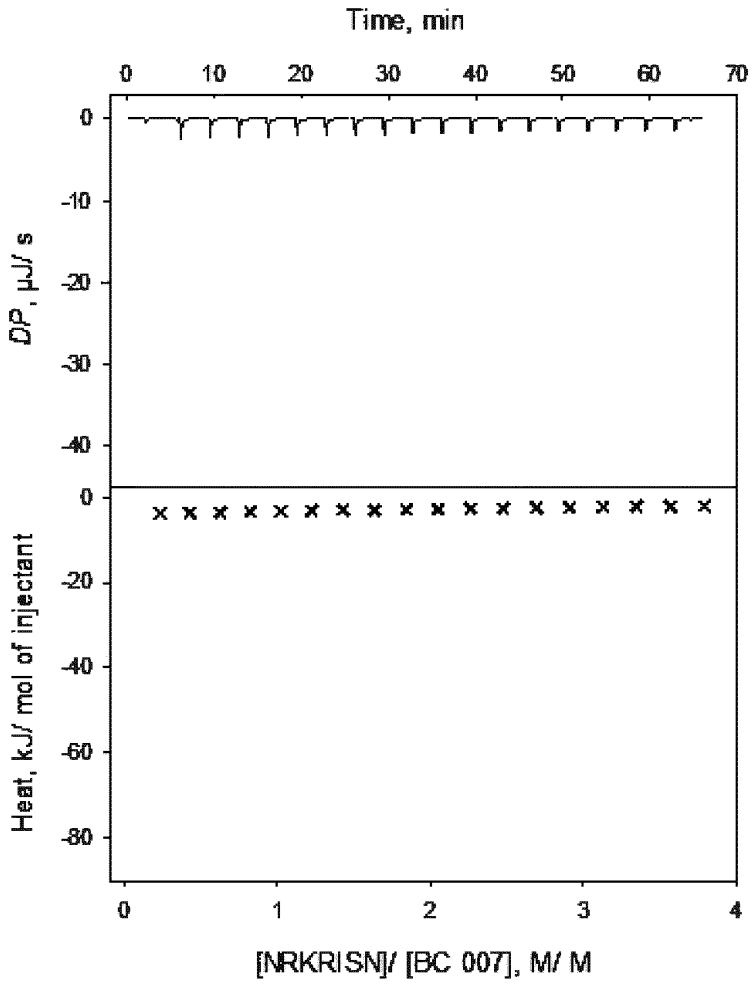

Time, min
0
10
20
30
40
50
60
70
0
-10
-20
-30
-40
DP, µJ/ s
0
-20
-40
-60
-80
Heat, kJ/ mol of injectant
0
1
2
3
4
[NRKRISN]/ [BC 007], M/ M

Figure 8

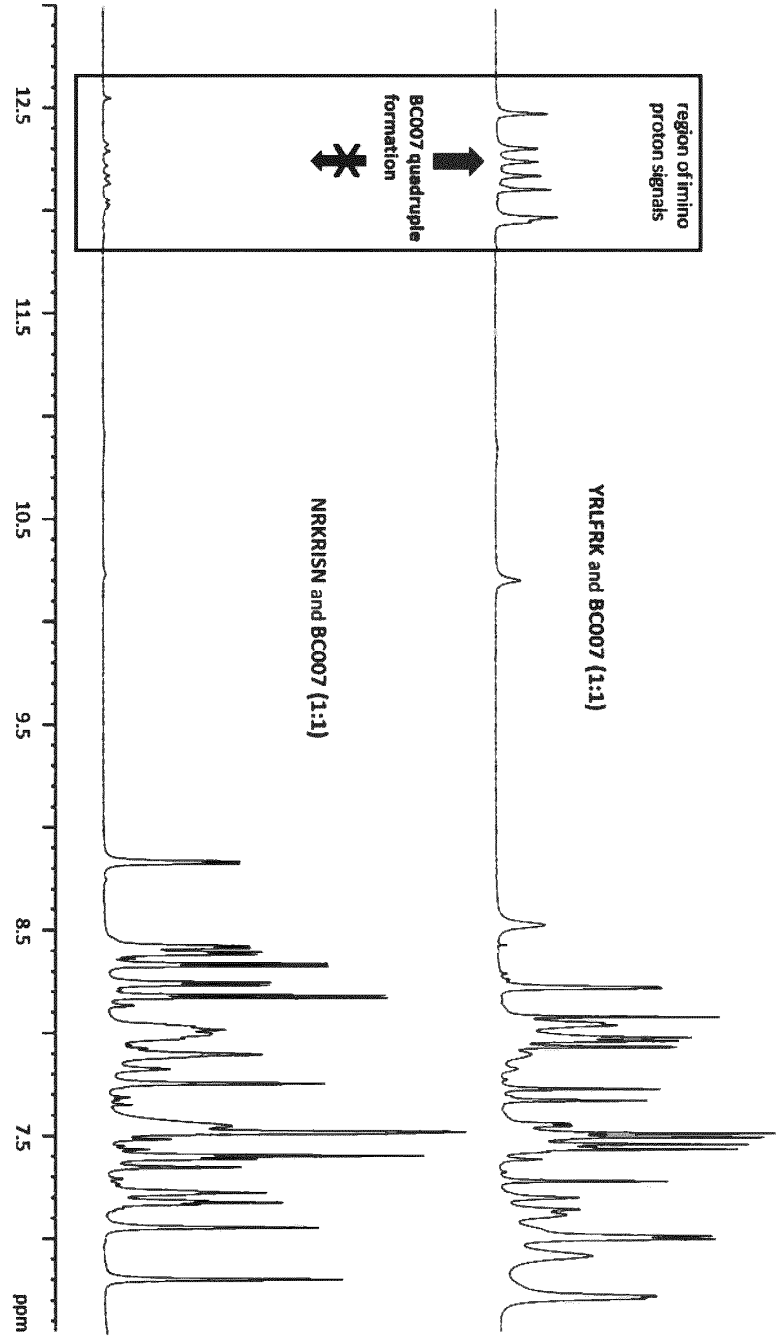
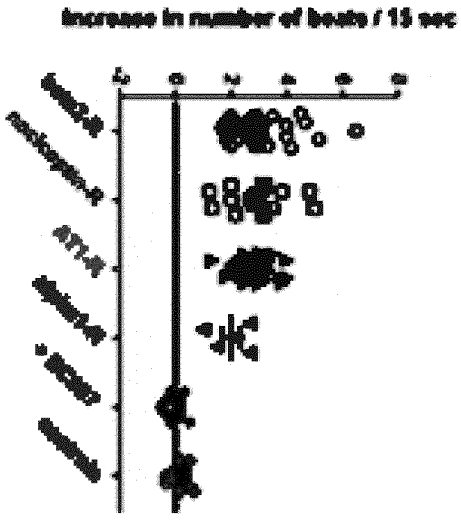

region of imino proton signals
BC007 quadruple formation
YRLFRK and BC007 (1:1)
NRKRISN and BC007 (1:1)
12.5
11.5
10.5
9.5
8.5
7.5
ppm

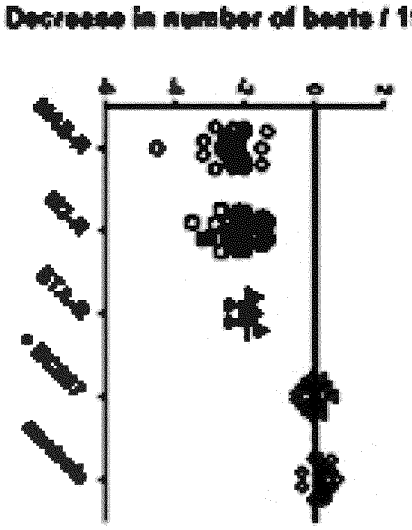
Figure 9

Patient no.	Gender	Age (years)	Running no.	Symptom clinic		Symptoms		Neuro-active pAABs	Vasoactive pAABs			Neuro- and vasoactive pAABs		RAS-specific pAABs	
				Neuro[a]	Cardiovasc[b]	Neuro[a]	Cardiovasc[b]	Muscarinic M2-pAAB	β2-pAAB[c]	α1-pAAB[d]	ETA-pAAB[e]	M2-pAAB[f]	AT1-pAAB[g]	MAS-pAAB[h]	
1	f	48	1	x	x	Fatigue, Alopecia, Anomic aphasia	Tachycardia	x	x		x	x	x	x	x
7	f	55	2	x	x	Fatigue, Alopecia	Tachycardia	x	x	x	x	x	x	x	x
11	f	39	3	x	x	Fatigue, Alopecia	Tachycardia	x	x			x	x	x	x
19	f	34	4	x	x	Fatigue, PoTS, Tremor	Tachycardia		x	x		x	x	x	x
22	f	34	5	x	x	Fatigue, Alopecia	Tachycardia		x	x		x	x	x	x
3	f	56	6	x	x	Fatigue, Attention deficit	Tachycardia,	x	x		x	x	x	x	x
21	f	28	7	x	x	Attention deficit, Tremor, Dysautonomia	Arrhythmia		x			x	x	x	x
18	f	53	8	x	x	Tremor, Attention deficit	Tachycardia		x			x	x		x
20	m	54	9	x	x	Attention deficit	Tachycardia, Hypertension							x	
14	f	57	10	x	x	Fatigue, Anomic aphasia	Arrhythmia, Hypertension	x	x				x	x	x
23	f	50	11	x	x	Eczema, Alopecia	Myocarditis		x		x		x	x	x
24	f	33	12	x	x	Fatigue, PoTS	n.s.	x	x	x			x	x	x
2	m	42	13	x	—	Fatigue, Alopecia	n.s.		x				x	x	x
4	m	50	14	x	—	Fatigue	n.s.		x				x	x	x
5	f	45	15	x	—	Fatigue	n.s.		x				x	x	x
6	f	36	16	x	—	Tremor, Alopecia, Dysautonomia	n.s.	x	x	x	x		x	x	x
9	f	50	17	x	—	Fatigue	n.s.	x	x				x	x	x
10	f	48	18	x	—	Fatigue	n.s.		x		x		x	x	x
12	f	53	19	x	—	Fatigue, Attention deficit	n.s.		x				x	x	x
15	f	46	20	x	—	Fatigue, Alopecia, Polyneuropathy	n.s.	x	x				x	x	x
17	f	49	21	x	—	Fatigue, PoTS, Tremor	n.s.		x				x		
25	f	58	22	x	—	Attention deficit, Neuropathy	n.s.		x		x		x	x	x
13	f	26	23	x	—	Fatigue	n.s.		x				x	x	x
8	m	71	24	—	—	Symptom free	Symptom free		x	x			x	x	x
16	m	54	25	—	—	Symptom free	Symptom free	x	x				x	x	x

Figure 10


Increase in number of beats / 15 sec

A


Decrease in number of beats / 15 sec.

B

Figure 11