

Type A SDF-1 binding nucleic acids

Name	nt.	Sequence: 5'-3'	Comp.
192-A10-001	38	GCUGUGAAAGCAACAUGUCAA-UGAAAGGUAGCGCAGC	
192-G10	38	GCUGUGAAAGUAACAUGUCAA-UGAAAGGUAAACACAGC	<
192-F10	38	GCUGUGAAAGUAACACGUCAA-UGAAAGGUAAACGCAGC	<
192-B11	38	GCUGUGAAAGUAACACGUCAA-UGAAAGGUAAACACAGC	=
192-C9	38	GCUGUAAGAGUAACAUGUCAA-UGAAAGGUAAACUACAGC	<
192-E10	38	GCUGUAAGAGUAACAAGUCAA-UGAAAGGUAAACUACAGC	<
192-C10	38	GCUGUGAAAGUAACAAGUCAA-UGAAAGGUAAACACAGC	=
192-D11	38	GCAGUGAAAGUAACAUGUCAA-UGAAAGGUAAACACAGC	<
192-G11	38	GCUGUGAAAGUAACAUGUCAA-UGAAAGGUAAACACUGC	<
192-H11	38	GCUAUGAAAGUAACAUGUCAA-UGAAAGGUAAACCAUAGC	<
192-D10	38	GCUGCGAAAGCGACAUGUCAA-UGAAAGGUAGCGCAGC	<<
192-E9	38	GCUGUGAAAGCAACAUGUCAA-UGAAAGGUAGCGCAGC	<<
192-H9	38	GCUGUGAAAGUAACAUGUCAA-UGAAAGGUAGCGCAGC	<<
191-A6	39	AGCGUGAAAGUAACACGUAAAAUGAAAGGUAAACACGCU	<

terminal nucleotides that may hybridize to each other (bold)

nucleotides which may mainly comprise a SDF-binding motif

nt.:= nucleotides [Geben Sie ein Zitat aus dem Dokument oder die Zusammenfassung eines interessanten Punkts ein. Sie können das Textfeld an einer beliebigen Stelle im Dokument positionieren. Verwenden Sie die Registerkarte 'Zeichentools', wenn Sie das Format des Textfelds 'Textzitat' ändern möchten.]

Comp.:= Clones were tested as aptamers in a competition binding assay vs. 192-A10-001

=:= equal binding affinity as 192-A10-001; <:= weaker binding affinity than 192-A1-001

<<:= much weaker binding affinity than 192-A10-001

Fig. 1

Derivatives of Type A SDF Binding Nucleic Acid 192-A10-001

Name	nt.	Sequence: 5'-3'	Comp.	PD: K _b [nM]	TAX IC ₅₀ [nM]
192-A10-001	38	GCUGUGAAAGCAACAUGUCAAAUGAAGGUAGC CGCAGC		1.5	0.1 - 0.2
192-A10-002	36	CUGUGAAAGCAACAUGUCAAAUGAAGGUAGC CGCAG	=		=
192-A10-003	34	UGUGAAAGCAACAUGUCAAAUGAAGGUAGC CGCA	<		<
192-A10-004	32	GUGAAAGCAACAUGUCAAAUGAAGGUAGC CGC	<<		<<
192-A10-005	30	UGAAAGCAACAUGUCAAAUGAAGGUAGC CG	<<		<<
192-A10-006	28	GAAAGCAACAUGUCAAAUGAAGGUAGC C	<<<		
192-A10-007	26	AAAGCAACAUGUCAAAUGAAGGUAGC	i. a.		

terminal nucleotides at the 5'- and the 3'-end that may hybridize to each other (bold) **nt.:=** nucleotides

nucleotides which may mainly comprise a SDF-binding motif **i. a.:=** inactive **:=** equal binding affinity as 192-A10-001

</<</<<<:= weaker (<), much weaker (<<) or very much weaker (<<<) binding affinity than 192-A1-001

Comp.:= Clones were tested as aptamers in a competition binding assay vs. 193-A10-001

PD.:= Clones were tested as aptamers in a pull-down binding assay

TAX:= Clones were tested as Spiegelmers in a cell culture *in vitro* chemotaxis assay

Fig. 2A

Derivatives of Type A SDF Binding Nucleic Acid192-A10-001

Name	nt.	Sequence: 5' -3'	Comp.	PD: K _D [nM]	TAX IC ₅₀ [nM]
192-A10-001	38	GCUGUG[AAAAGCAACAUGUCAAAUGAAAAGGUAGC]CGCAGC		1.5	0.1 - 0.2
192-A10-002	36	CUGUG[AAAAGCAACAUGUCAAAUGAAAAGGUAGC]CGCAG	=		=
192-A10-008	36	GCGUG[AAAAGCAACAUGUCAAAUGAAAAGGUAGC]CGCGC	=	1.5	=
192-A10-015	36	GCGCG[AAAAGCAACAUGUCAAAUGAAAAGGUAGC]CGCGC	<	4.6	
192-A10-014	34	GCGG[AAAAGCAACAUGUCAAAUGAAAAGGUAGC]CCGC	<	8.0	=
192-A10-016	34	CGUG[AAAAGCAACAUGUCAAAUGAAAAGGUAGC]CGCG	<		
192-A10-017	34	GCGC[AAAAGCAACAUGUCAAAUGAAAAGGUAGC]GUGC	i. a.		
192-A10-018	34	GUGC[AAAAGCAACAUGUCAAAUGAAAAGGUAGC]GCGC	<<<		
192-A10-019	34	CGCG[AAAAGCAACAUGUCAAAUGAAAAGGUAGC]CGUG	<<		
192-A10-020	34	GGGC[AAAAGCAACAUGUCAAAUGAAAAGGUAGC]GCC	<<*		
192-A10-021	34	GGCC[AAAAGCAACAUGUCAAAUGAAAAGGUAGC]GGCC	<<*		
192-A10-022	34	GCCC[AAAAGCAACAUGUCAAAUGAAAAGGUAGC]GGGC	<<*		
192-A10-023	34	CCCC[AAAAGCAACAUGUCAAAUGAAAAGGUAGC]GGGG	<<*		

terminal nucleotides at the 5'- and the 3'-end that may hybridize to each other (bold)

nt.:= nucleotides

nucleotides which may mainly comprise a SDF-binding motif

i. a.:= inactive

:= equal binding affinity as 192-A10-001/ -008

</<</<<<:= weaker (<), much weaker (<<) or very much weaker (<<<) binding affinity than 192-A1-001/ -008

Comp.:= Clones were tested as aptamers in a competition binding assay vs. 192-A10-001 (* = except from 192-A10-020, -021, -022, and -023 which were tested vs. 193-A10-008 that has the identical binding affinity to SDF-1 as 192-A10-001)

PD.:= Clones were tested as aptamers in a pull-down binding assay

TAX:= Clones were tested as Spiegelmers in a cell culture *in vitro* chemotaxis assay

Fig. 2B

Type B SDF-1 binding nucleic acids

Name	nt.	Sequence: 5' -3'	C.
193-C2-001	47	AGCGUG GUGUGAUCUAGAUGUAGUGGCUGAUCCUAGUCAGG UACGCU	+
193-G2-001	47	AGCGUG GUGUGAUCUAGAUGUAUUGGCUGAUCCUAGUCAGG UACGCU	+
193-F2-001	47	AGCGUG GUGUGAUCUAGAUGUAAUGGCUGAUCCUAGUCAGG UGCGCU	+
193-G1-002	45	GCGAG GUGUGAUCUAGAUGUAGUGGCUGAUCCUAGUCAGG UGCGC	<<
193-D2-002	45	GCGUG GUGUGAUCUAGAUGUAGUGGCUGAUCCUAGUCAGG UGCGC	<
193-A1-002	45	GCAUG GUGUGAUCUAGAUGUAGUGGCUGAUCCUAGUCAGG UGCCC	<<<
193-D3-002	45	GCGUG GUGUGAUCUAGAUGUAAUGGCUGAUCCUAGUCAGG GACGC	<
193-B3-002	45	GCGUG GUGUGAUCUAGAUGUAGAGGCUGAUCCUAGUCAGG UACGC	<<
193-H3-002	45	GCGUG GUGUGAUCUAGAUGUAAAGGCUGAUCCUAGUCAGG UACGC	<
193-E3-002	45	GCGUG GUGUGAUCUAGAUGUAGUGGCUGUCCUAGUCAGG UAUGC	<<
193-D1-002	45	GCGUG GUGUGAUCUAGAUGUAGUGGCUGAUCCUAGUUAGG UACGC	<<<

terminal nucleotides that may hybridize to each other (bold)

nucleotides which may mainly comprise a SDF-binding motif

nt.:= nucleotides

C.:= Clones C2, G2, and F2 were tested as aptamers in a competition binding assay vs. 192-A10-001; all other clones were tested as aptamers in a competition binding assay vs. 193-G2-012 that has the identical binding affinity to SDF-1 as 193-G2-001 (see Fig. 4B)

+= better binding affinity than 192-A10-001

</<</<<<:= weaker (<), much weaker (<<) or very much weaker (<<<) binding affinity than 193-G2-001/ -012

Fig. 3

Derivatives of Type B SDF Binding Nucleic Acids 193-C2/G2-001

Name	nt.	Sequence: 5'-3'	Comp.	PD K _b [nM]	Biacore K _b [nM]
193-G2-001	47	AGCGUGGUGUGAUCUAGAUGAUUGGCUGAUCCUAGUCAGGUAACGCU		0.3	0.5
193-C2-001	47	AGCGUGGUGUGAUCUAGAUGAGUGGCUGAUCCUAGUCAGGUAACGCU	=		0.6
193-C2-002	45	GCUGUGGUGUGAUCUAGAUGAGUGGCUGAUCCUAGUCAGGUAACGC	=		0.8
193-C2-003	43	CGUGGUGUGAUCUAGAUGAGUGGCUGAUCCUAGUCAGGUAACG	<		
193-C2-004	41	GUGGUGUGAUCUAGAUGAGUGGCUGAUCCUAGUCAGGUAAC	<<		
193-C2-005	39	UGGUGUGAUCUAGAUGAGUGGCUGAUCCUAGUCAGGUA	<<<		
193-C2-006	37	GUGUGAUCUAGAUGAGUGGCUGAUCCUAGUCAGGU	<<<		
193-C2-007	35	GUGUGAUCUAGAUGAGUGGCUGAUCCUAGUCAGG	i. a.		

terminal nucleotides at the 5'- and the 3'-end that may hybridize to each other (bold) **nt.:=** nucleotides
nucleotides which may mainly comprise a SDF-binding motif **i.a.:=** inactive **:=** equal binding affinity as 193-G2-001
</<</<<<:= weaker (<), much weaker (<<) or very much weaker (<<<) binding affinity than 193-G2-001
Comp.:= Clones were tested as aptamers in a competition binding assay vs. 193-G2-001
PD.:= Clones were tested as aptamers in a pull-down binding assay

Fig. 4A

Derivatives of Type B SDF Binding Nucleic Acid193-C2/G2-001

Name	nt.	Sequence: 5'-3'	Comp.	PD K _b [nM]	Biacore K _b [nM]
193-G2-001	47	AGCGUGGUGUGAUCUAGAUGUAUUGGCUGAUCCUAGUCAGGUAACGCU		0.3	0.5
193-G2-012	45	GGCGUGGUGUGAUCUAGAUGUAUUGGCUGAUCCUAGUCAGGUAACGC	=	0.3	
193-G2-013	45	GGCGCGGUGUGAUCUAGAUGUAUUGGCUGAUCCUAGUCAGGCGCGGC	<<	5.3	
193-G2-014	43	GGCGGUGUGAUCUAGAUGUAUUGGCUGAUCCUAGUCAGGCGCGC	<<	4.7	
193-G2-015	43	GGGCGGUGUGAUCUAGAUGUAUUGGCUGAUCCUAGUCAGGCGCC	<<*	4.5	
193-G2-016	43	GGCCCGGUGUGAUCUAGAUGUAUUGGCUGAUCCUAGUCAGGCGCC	<<*	4.2	
193-G2-017	43	GGCCCGGUGUGAUCUAGAUGUAUUGGCUGAUCCUAGUCAGGCGGC	<<*	4.2	

terminal nucleotides at the 5'- and the 3'-end that may hybridize to each other (bold)

nt.:= nucleotides

nucleotides which may mainly comprise a SDF-binding motif

:= equal binding affinity as 193-G2-001/ -012

</<</<<<:= weaker (<), much weaker (<<) or very much weaker (<<<) binding affinity than 193-G2-001 and 193-G2-012, respectively

Comp.:= Clones were tested as aptamers in a competition binding assay vs. 193-G2-001 (* = except from 193-G2-015, -016, -017 which were tested in a competition binding assay vs. 193-G2-012 that has the identical binding affinity to SDF-1 as 193-G2-001)

PD.:= Clones were tested as aptamers in a pull-down binding assay

Fig. 4B

Type C SDF-1 binding nucleic acids

Name	nt.	Sequence: 5'-3'	Comp.
197-B2	39	GUGCUGCGGGGGUUVAGGGCUAGAAAGUCGGCCUGCAGCAC	<
191-D5-001	39	AGCGUGGCGAGGUUVAGGGCUAGAAAGUCGGUCGACACGCU	<
197-H1	39	GUGUUGCGGAGGUUVAGGGCUAGAAAGUCGGUCAGCAGCAC	<
190-D3	48	CGUGCGGCCUAAAGAGGUUVAGGGCUUAAAAGUCGGUCUUUGGCCAAACAG	<<
190-A3-001	48	CGUGCGGCUUGAGAUAGGGUUVAGGGCUUAAAAGUCGGCUGAUUCUCACG	<
190-A3-001*	48	CGUGCGGCUUGAGAUAGGGUUVAGGGCUUAAAAGUCGGCUGAUUCUCACG	<
190-A2	48	CGUGAUUGGUGAGGGUUVAGGGCUUAGAAAGUCGGCCUUGUCCAGUCACG	<<
191-A5	39	AGCGUGAAGGGUUVAGGGCUCGAAAGUCGGCUGACACGCU	<<
197-H3	39	GUGCUGCGGGGGUUVAGGGCUCGAAAGUCGGCCCGCAGCAC	<
197-B1	39	GUGUUCCCGGGUUVAGGGCUUAGAAAGUCGGCCGGCAGCAC	<<
197-E3	39	GUGUUGCAGGGUUVAGGGCUUAGAAAGUCGGCCUGCAGCAC	<
197-H2	39	GUGCUGCGGGGGUUVAGGGCUCAAAAGUCGGCCUGCAGCAC	<<
197-D1	38	GUGCUGCCGGGGUUVAGGGCUAA-AGUCGGCCGACAGCAC	<<
197-D2	39	GUGCUGUGGGGGUCAGGGCUAGAAAGUCGGCCUGCAGCAC	<<

terminal nucleotides that may hybridize to each other (bold)

nucleotides which may mainly comprise a SDF-binding motif

nt.:= nucleotides Comp.:= Clones were tested as aptamers in a competition binding assay vs. 192-A10-001
:= equal binding affinity as 192-A10; <:= weaker binding affinity than 192-A10 <<:= much weaker binding affinity than 192-A10
*:= alternative hybridization

Fig. 5

Derivatives of Type C SDF Binding Nucleic Acid 190-A3-001

Name	nt.	Sequence: 5'-3'	Comp.
190-A3-001	48	CGUGCGCUUGAGAUAGG GGUUAGGGCUUAAAGUCGG CUGAUUC UCACG	
190-A3-001 *	48	CGUGCGCUUGAGAUAGG GGUUAGGGCUUAAAGUCGG CUGAUUC UCACG	
190-A3-003	38	UGAGAUAGG GGUUAGGGCUUAAAGUCGG CUGAUUC UCA	=
190-A3-004	36	GAGAUAGG GGUUAGGGCUUAAAGUCGG CUGAUUC UC	=
190-A3-007	29	GG GGUUAGGGCUUAAAGUCGG CUGAUUCU	<<<

terminal nucleotides at the 5'- and the 3'-end that may hybridize to each other (bold) nt.:= nucleotides

nucleotides which may mainly comprise a SDF-binding motif := equal binding affinity as 190-A3-001

</<</<<:= weaker (<), much weaker (<<) or very much weaker (<<<) binding affinity than 190-A3-001

Comp.:= Clones were tested as aptamers in a competition binding assay vs. 190-A3-001

*:= alternative hybridization of the terminal nucleotides

Fig. 6

Derivatives of Type C SDF Binding Nucleic Acid 191-D5-001

Name	nt.	Sequence: 5'-3'	Comp. vs. 191-D5-001	Comp. vs. 191-D5-007	Biacore K _D [nM]
191-D5-001	39	AGCGUGGCCGA GGUAGGGCUAGAA GUCGG UCGACACGCU		<	0.73
191-D5-002	37	GCGUGGCCGA GGUAGGGCUAGAA GUCGG UCGACACGC	=		
191-D5-003	35	CGUGGCCGA GGUAGGGCUAGAA GUCGG UCGACACG	=		
191-D5-004	33	CG-GGCCGA GGUAGGGCUAGAA GUCGG UCGAC-CG	<		
191-D5-005	33	CG-GGCCGA GGUAGGGCUAGAA GUCGG UCGCC-CG	=		
191-D5-006	31	CG--GCCGA GGUAGGGCUAGAA GUCGG UCGC--CG	=		
191-D5-007	29	CG--G-GA GGUAGGGCUAGAA GUCGG UC-C--CG	+		0.75
191-D5-010	27	G--G-GA GGUAGGGCUAGAA GUCGG UC-C--C		<	

terminal nucleotides at the 5'- and the 3'-end that may hybridize to each other (bold) **nt.:= nucleotides**

nucleotides which may mainly comprise a SDF-binding motif **:=** equal binding affinity as 191-D5-001/ -007

</<</<<<:= weaker (<), much weaker (<<) or very much weaker (<<<) binding affinity than 191-D5-001/ -007

Comp.:= Clones were tested as aptamers in a competition binding assay vs. 191-D5-001 or 191-D5-007 whereas both clones have the identical binding affinity to SDF-1 as 191-D5-001

Fig. 7A

Derivatives of Type C SDF Binding Nucleic Acid 191-D5-001

Name	nt.	Sequence: 5'-3'	Comp. vs. 191-D5-007
191-D5-007	29	CG---G- GA GGUAGGGCUAGAAGUCG UC-C--CG	
191-D5-010	27	G---G- GA GGUAGGGCUAGAAGUCG UC-C--C	<
191-D5-017	27	CCGC GGU AGGGCUAGAAGUCG GCGG	<
191-D5-029	27	CCCG GGU AGGGCUAGAAGUCG CGGG	<
191-D5-024	27	GGCG GGU AGGGCUAGAAGUCG CGCC	<
191-D5-017-29a	29	CCCGC GGU AGGGCUAGAAGUCG GCGGG	<
191-D5-017-29b	29	GCCGC GGU AGGGCUAGAAGUCG GCGGC	<
191-D5-019-29a	29	CCCCG GGU AGGGCUAGAAGUCG CGGGG	<
191-D5-024-29a	29	CGGCG GGU AGGGCUAGAAGUCG CGCCG	=
191-D5-024-29b	29	GGGCG GGU AGGGCUAGAAGUCG CGCCC	=

terminal nucleotides at the 5'- and the 3'-end that may hybridize to each other (bold) nt.:= nucleotides

nucleotides which may mainly comprise a SDF-binding motif

==: equal binding affinity as 191-D5-007

</<</<<<:= weaker (<), much weaker (<<) or very much weaker (<<<) binding affinity than 191-D5-007

Comp.:= Clones were tested as aptamers in a competition binding assay vs. 191-D5-007

Fig. 7B

Derivatives of Type C SDF Binding Nucleic Acid197-B2

Name	nt.	Sequence: 5'-3'	Comp. vs. 197-B2	Comp. vs. 191-D5-007	TAX IC ₅₀ [nM]
197-B2	39	GUGCUGCGGGGGUUAGGGCUAGAAAGUCGGCCUGCAGCAC		=	0.1-0.2
197-B2-001	37	UGCUGCGGGGGUUAGGGCUAGAAAGUCGGCCUGCAGCA	=		
197-B2-002	35	GCUGCGGGGGUUAGGGCUAGAAAGUCGGCCUGCAGC	=		
197-B2-003	33	CUGCGGGGGUUAGGGCUAGAAAGUCGGCCUGCAG	=		
197-B2-004	31	UGCUGGGGUAGGGCUAGAAAGUCGGCCUGCA	=		
197-B2-005	29	GCGGGGGUUAGGGCUAGAAAGUCGGCCUGC	=		
197-B2-006	29	GCCGGGGUUAGGGCUAGAAAGUCGGCCGGC	=	=	0.1-0.2
197-B2-006-31a	31	GgcccGGGUAGGGCUAGAAAGUCGGCCGGCC		=	
197-B2-006-31b	31	CgcccGGGUAGGGCUAGAAAGUCGGCCGGCG		=	

terminal nucleotides at the 5'- and the 3'-end that may hybridize to each other (bold) **nt.:= nucleotides**

nucleotides which may mainly comprise a SDF-binding motif **i.a.:= inactive**

:= equal binding affinity as 197-B2 or 191-D5-007

</<</<<<:= weaker (<), much weaker (<<) or very much weaker (<<<) binding affinity than as 197-B2 or 191-D5-007

Comp.:= Clones were tested as aptamers in a competition binding assay vs. 197-B2 or 191-D5-007 whereas both clones have the identical binding affinity to SDF-1

TAX:= Clones were tested as Spiegelmers in a cell culture *in vitro* chemotaxis assay

Fig. 8

Other SDF-1 Binding Nucleic Acids (Type D SDF-1 Binding Nucleic Acids)

Name	nt.	Sequence: 5' -3'	PD K _b [nM]
194-A2-001	48	CGUGGUCGCGUUGUGUCAGGUCUAUUCGCCCGGUGCAGGGCAU CCGCG	12.0
196-B12-003	49	GCAUGUGAGACGCGGACGUGAUAGGACAGAGCUGAUCCCGCUCAGGUGAG	7.6
196-B12-004	49	CAACAGCAGUGUGACGCGGACGUGAUAGGACAGAGCUGAUCCCGCUCAG	5.3

terminal nucleotides at the 5'- and the 3'-end that may hybridize to each other (bold) nt.:= nucleotides

PD.:= Clones were tested as aptamers in a pull-down binding assay

Fig. 9

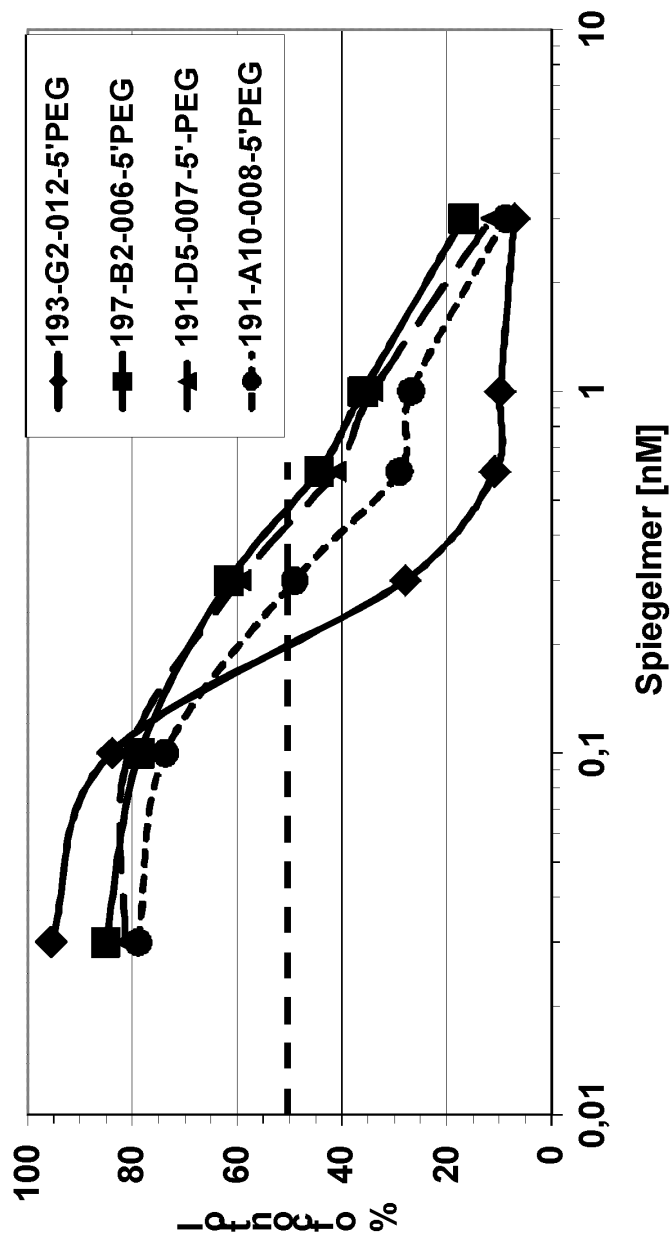
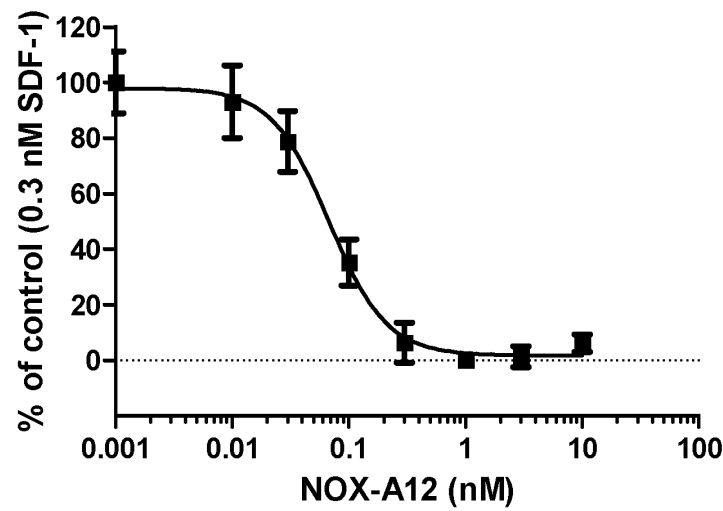


Fig. 10

A



B

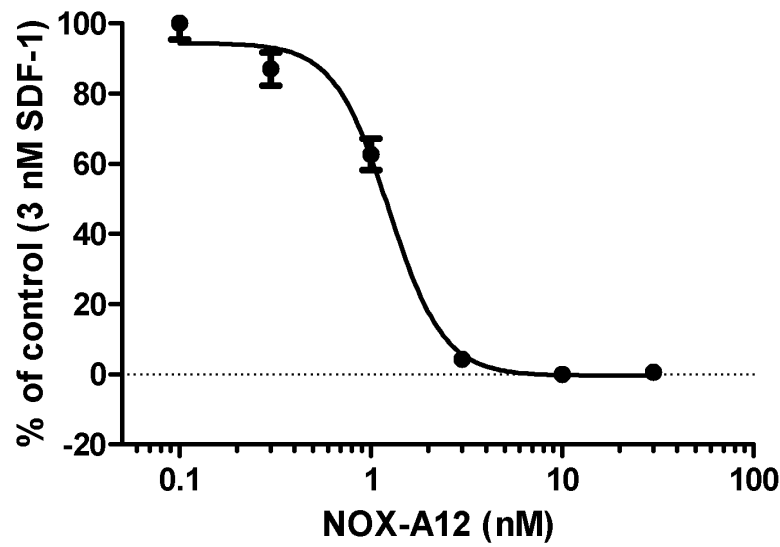


Fig. 11

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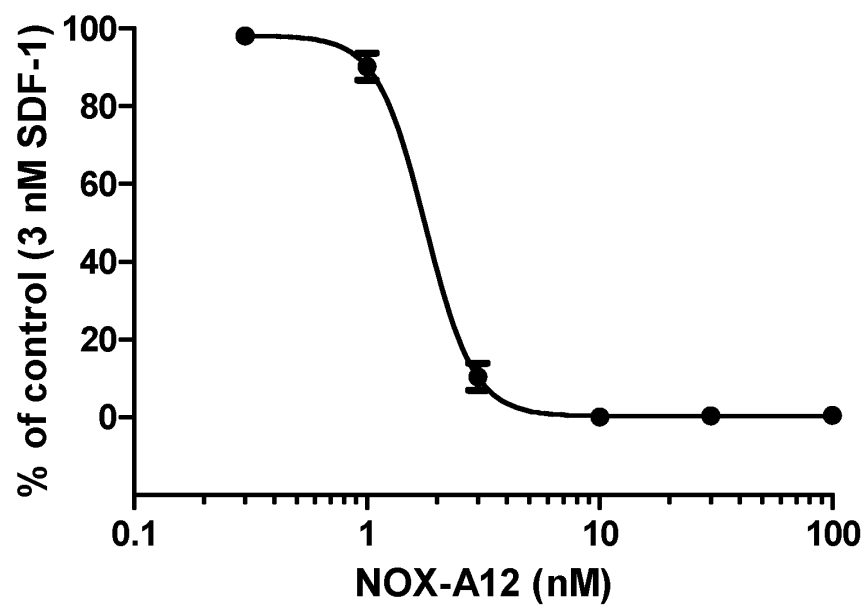
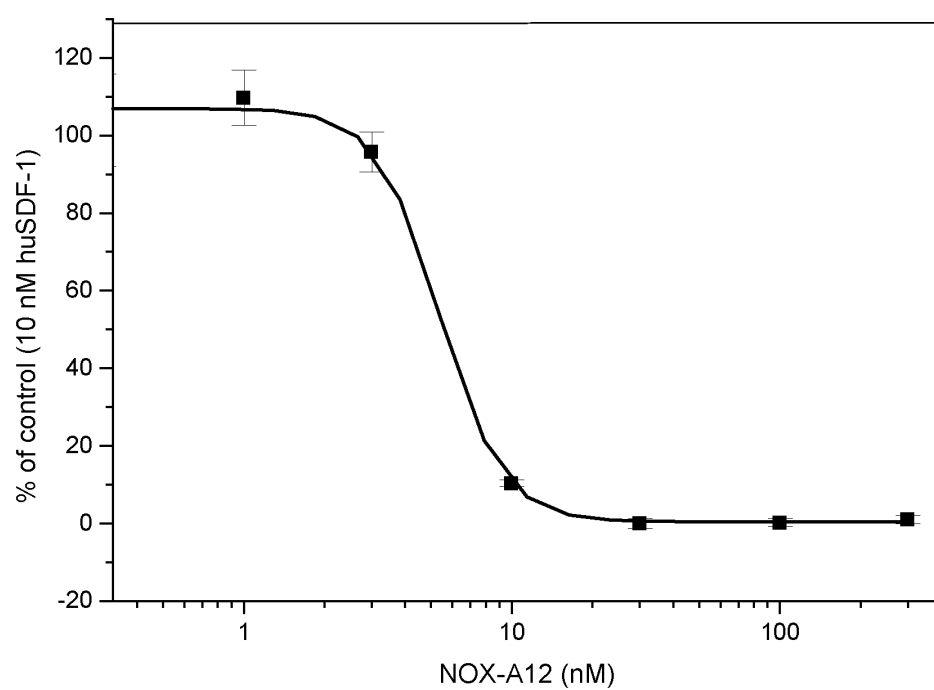


Fig. 12

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**Fig. 13**

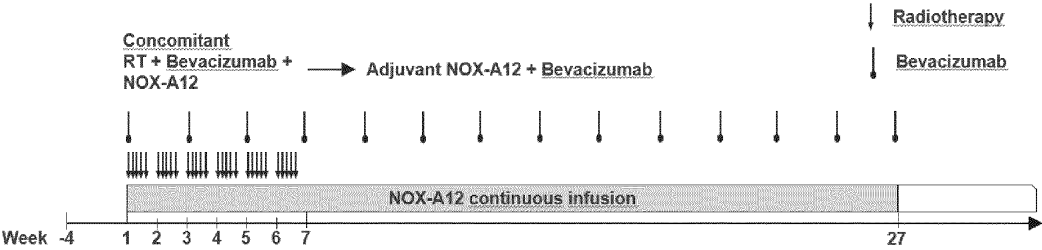


Fig. 14

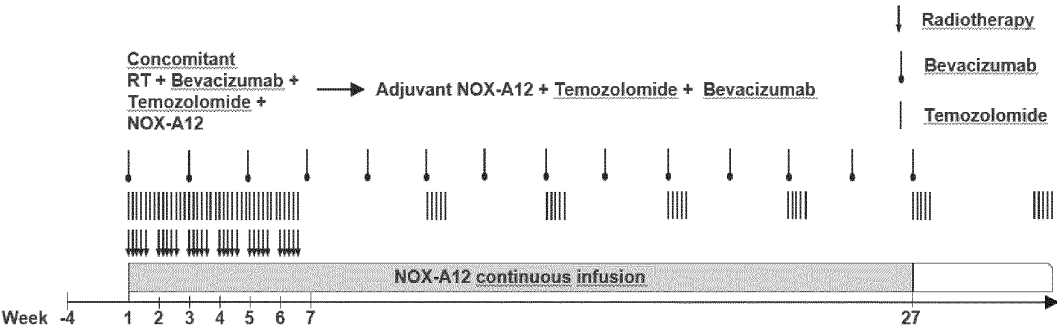


Fig. 15

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MEGISIYTS DNYTEEMGSGDYDSMKEPCFREENANFNKIFLPTIYSIIFLTGIVGNGLVILVMGYQKKL
RSMTDKYRLHLSVADLLFVITLPFWAVDAVANWYFGNFLCKAVHVIYTVNLYSSVLILAFISLDRY
LAIVHATNSQRPRKLLAEKV VYVGWIPALLLTIPDFIFANVSEADDRYICDRFYPNDLWVVVFQFQ
HIMVGLILPGIVILSCYCIISKLSHSKGHQKRKALKTTVILILAFFACWLPYYIGISIDSFILLEIHKQGCE
FENTVHKWISITEALAFFHCCLNPILYAFLGAKFKTSAQHALTSVSRGSSLKILSKGKRGGHSSVSTES
ESSSFH (SEQ ID NO: 243)

Fig. 16

MDLHLFDYSEPGNFSDISWPCNSSDCIVVDTVMCPNMPNKS VLLYTL SFIYIFIFVIGMIANSVVVWV
NIQAKTTGYDTHCYILNLAIDLWVVLTPVWVVS LVQHNQWPMGELTCKVTHLIFSINLFGSIFFLT
CMSVDRLYSITYFTNTPSSRKKMVR RVVCILVWLLAFCVSLPDTYYLKT VTSASNNETYCRSFYPEH
SIKEWLIGMELVS VVLGFAVPFSIIAVFYFLLAR AISASSDQEKHSSRKIIFS YVVVFLVCWLPYHVAV
LLDIFSILHYIPFTCRLEHALFTALHVTQCLSLVHCCVNPVLYSFINRNYRYELMKAFIFKYSAKTGLT
KLIDASRVSETEYSALEQSTK (SEQ ID NO: 244)

Fig. 17

MVSYWDTGVLLCALLSCLLLTGSSSGSKLKDPELSLKGTQHIMQAGQTLHLQCRGEAAHKWSLPE
MVSKESERLSITKSACGRNGKQFCSTLTLNTAQANHTGFYSCKYLAVPTSKKKETESAIYIFISDTGR
PFVEMYSEIPEIIHMTGRELVIPCRVTSPNITVTLKKFPLDTLIPDGKRIIWDSRKGFHISNATYKEIGL
LTCEATVNGHLYKTNLYLTHRQTNTIIDVQISTPRPVKLLRGHTLVLNCTATTPLNTRVQMTWSYPDE
KNKRASVRRRIDQSNSHANIFYSVLTIDKMQNKDKGLYTCRVRSGPSFKSVNTSVHIYDKAFITVKH
RKQQVLETVAGKRSYRLSMKVKAFFSPEVVWLKDGLPATEKSARYLTRGYSIIKDVTEEDAGNYT
ILLSIKQSNVFNLTATLIVNVKPQIYEKAVSSFPDPALYPLGSRQILTCTAYGIPQPTIKWFWHPCNH
NHSEARCDFCSNNEESFILDADSNMGNRIESITQRMATIEGKNKMASTLVVADSRISGIYICIASNKVG
TVGRNISFYITDVPNGFHVNLEKMPTEGEDLKL SCTVNKFLYRDVTWILLRTVNNRTMHYSISKQK
MAITKEHSITLNLTIMNVSLQDSGTACRARNVYTGEIILQKKEITIRDQEAPYLLRNLSDHTVAISS
TTLDCHANGVPEPQITWFKNNHKIQQEPGILPGSSTLFIERVTEEDEGVYHCKATNQKGSVESSAY
LTVQGTSDKSNLELITLTCTCVAATLFWLLTLFIRKMKRSSSEIKTDYLSIIMDPDEVPLDEQCERLP
YDASKWEFARERLKLKSLGRGAFGKVQVQASAFGIKKSPTCRTVAVKMLKEGATASEYKALMTEL
KILTHIGHHLNVVNLLGACTKQGGPLMVIVEYCKYGNLSNYLKS KRDLFFLNKDAALHMEPKKEK
MEPGLEQGKKPRLDSVTSSSEFASSGFQEDKSLSDVEEEEDSDGFYKEPITMEDLISYSFQVARGMEF
LSSRKCIHRDLAARNILLSENN VVKICDFGLARDIYKNPDYVRKGDTRLPLKWMAPESIFDKIYSTKS
DVWSYGVLLWEIFSLGGSPYPGVQMDEDFCSRLREGMRMRAPYSTPEIYQIMLDCWHRDPKERP
RFAELVEKLGDLLQANVQQDGKDYIPINAILTGNSGFTYSTPAFSEDFKESISAPKFNSGSSDDVRY
VNAFKFMSLERIKTFEELLPNATSMFDDYQGDSTLLASPMLKRFTWTDSPKASLKIDLRVTSKSK
ESGLSDVSRPSFCHSSCGHVSEGKRRFTYDHAELERKIACCSPPPDYN SVVLYSTPPI (SEQ ID NO:
245)

Fig. 18

MQSKVLLAVALWLCVETRAASVGLPSVSLDLPRLSIQKDILTIKANTTLQITCRGQRDLDWLWPNN
QSGSEQRVEVTECSDGLFCKTLTIPKVIGNDTGAYKCFYRETDLASVIYVYVQDYRSPFIASVSDQH
GVVYITENKNKTVVIPCLGSISNLNVSLCARYPEKRFVPDGNRISWDSKKGFTIPSYMISYAGMVFCE
AKINDESYQSIMYIVVVVGYRIYDVVLSPSHGIELSVGEKLVNCTARTELNVGIDFNWEYPSSKHQ
HKKLVNRDLKTQSGSEMKKFLSTLTIDGVTRSDQGLYTCAASSGLMTKKNSTFVRVHEKPFVAFGS
GMESLVEATVGERVRIPAKYLGYPPEIKWYKNGIPLESNHTIKAGHVLTIMEVSRDTGNYTVILT
NPISKEKQSHVVSLVVYVPPQIGEKSLISPVDSYQYGTTQTLTCTVYAIPPPHHIHWYWQLEEECANE
PSQAVSVTNPPYPCEEWRSVEDFQGGNKIEVNKNQFALIEGKNKTVSTLVIQAANVSALYKCEAVNK
VGRGERVISFHVTRGPEITLQPDMQPTEQESVSLWCTADRSTFENLTWYKLGPPQPLPIHVGELPTPVC
KNLDTLWKLNATMFSNSTNDILIMELKNASLQDQGDYVCLAQDRKTKKRHCVVRQLTVLERVAPT
ITGNLENQTTSIGESIEVSCTASGNPPPQIMWFKDNETLVEDSGIVLKDGNRNLTI RVRKEDEGLYT
CQACSVLGCAKVEAFFIIEGAQEKTNLEIILVGTAVIAMFFWLLLVIILRTVKRANGGELKTGYLSIV
MDPDELPLDEHCERLPYDASKWEFPRDRLKLGKPLGRGAFGQVIEADAFGIDKTATCRTVAVKML
KEGATHSEHRALMSELKILIHIGHHLNVVNLLGACTKPGGPLMVIVEFCKFGNLSTYLRSKRNEFPV
YKTKGARFRQGDYVGAIPVDLKRRLDSITSSQSSASSGFVEEKSLSDVEEEEAPEDLYKDFTLEHL
ICYSFQVAKGMEFLASRK (SEQ ID NO: 246)

Fig. 19



Fig. 20

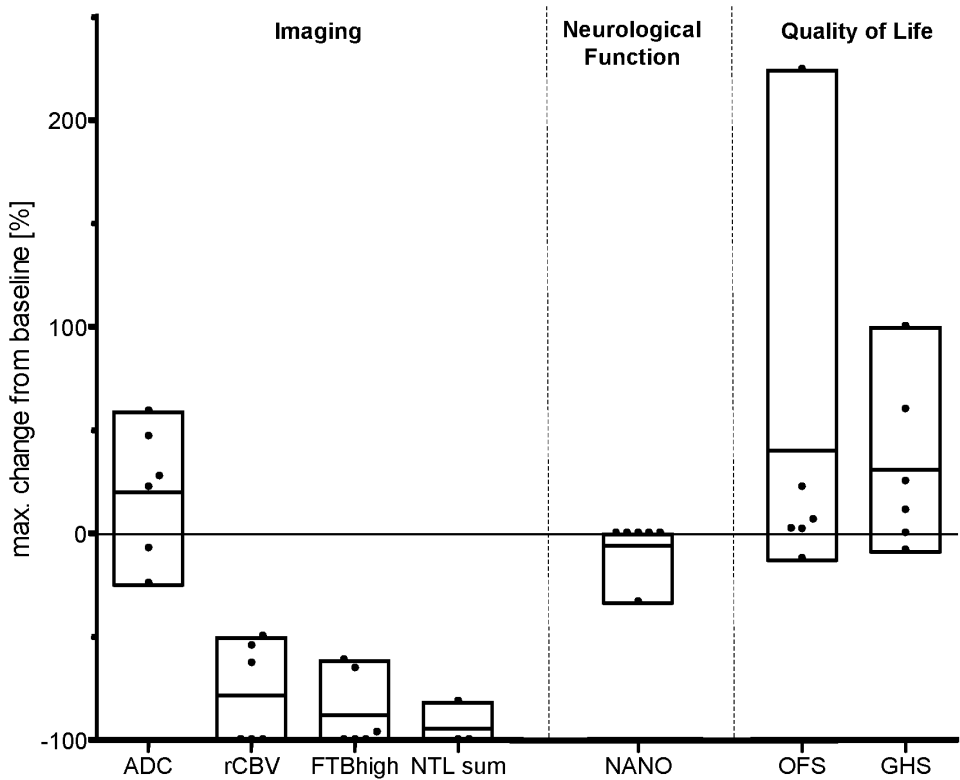


Fig. 21

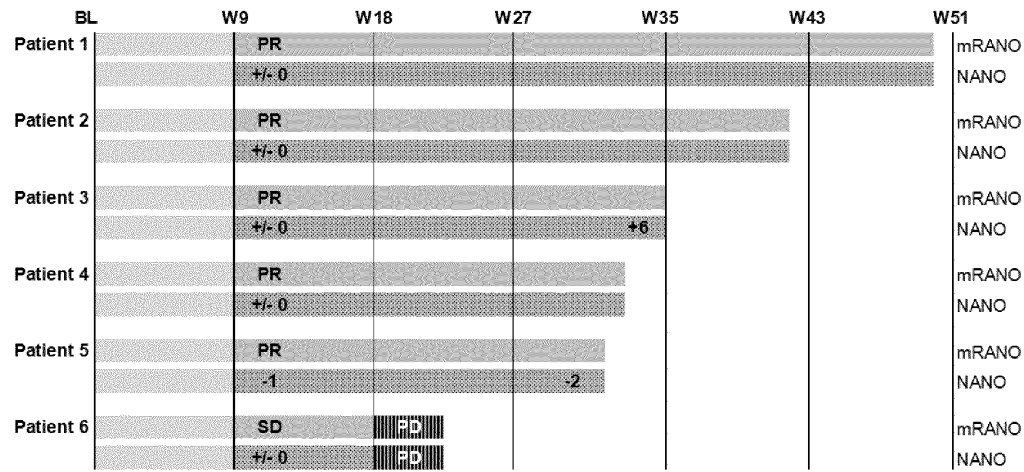


Fig. 22

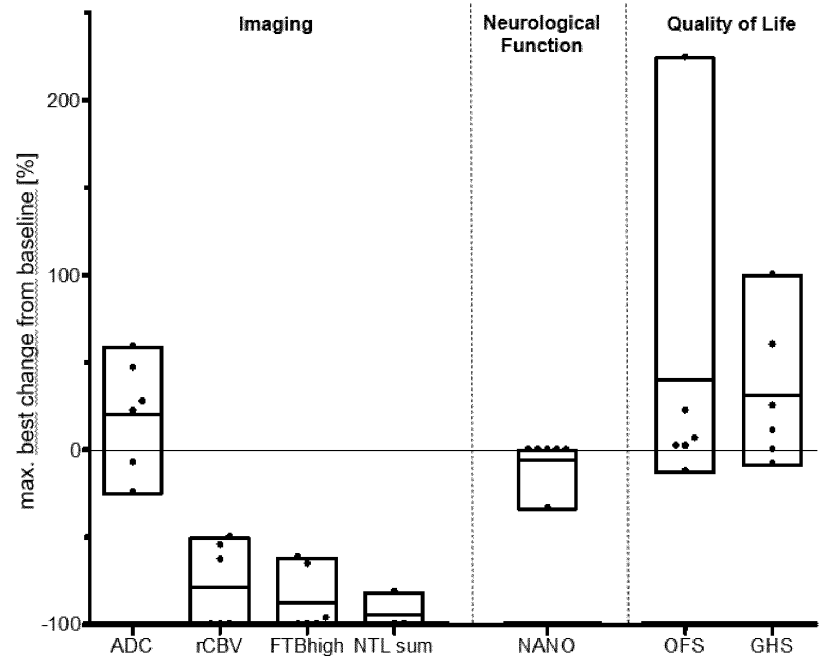


Fig. 23

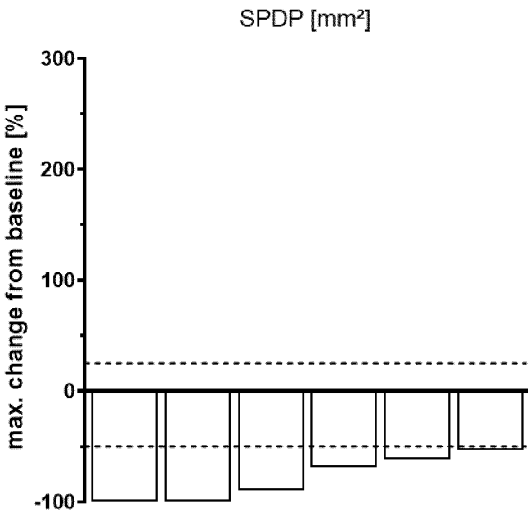


Fig. 24

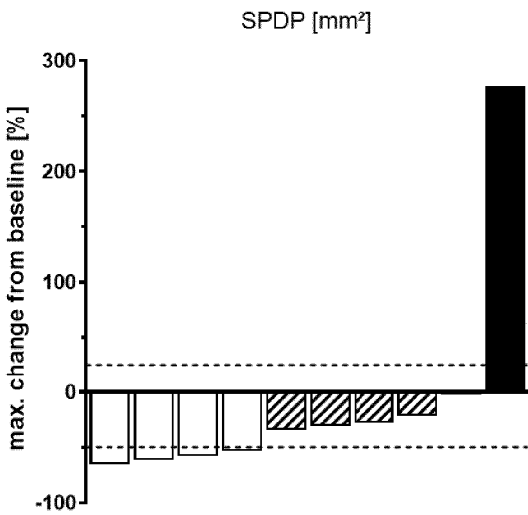


Fig. 25

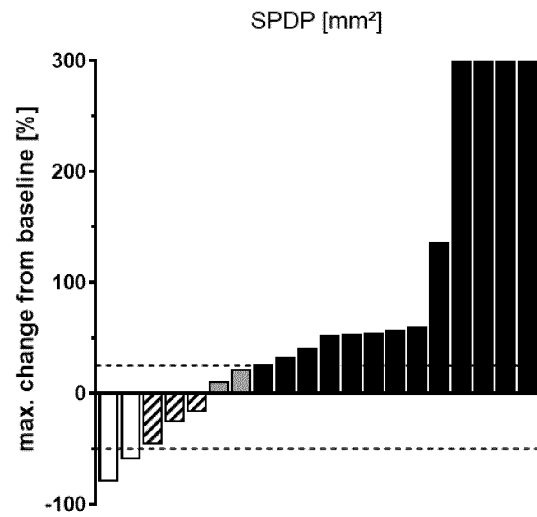


Fig. 26

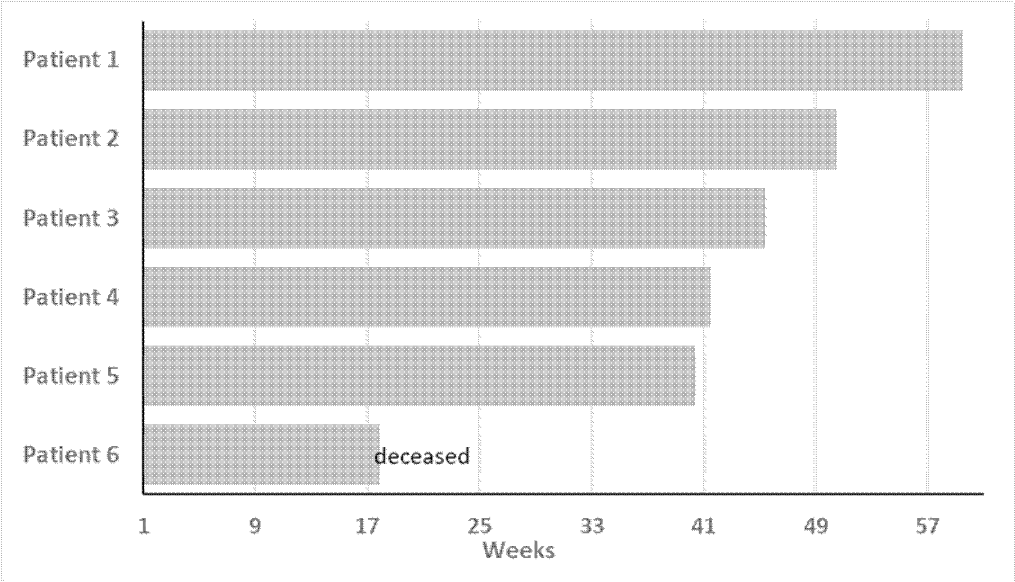


Fig. 27

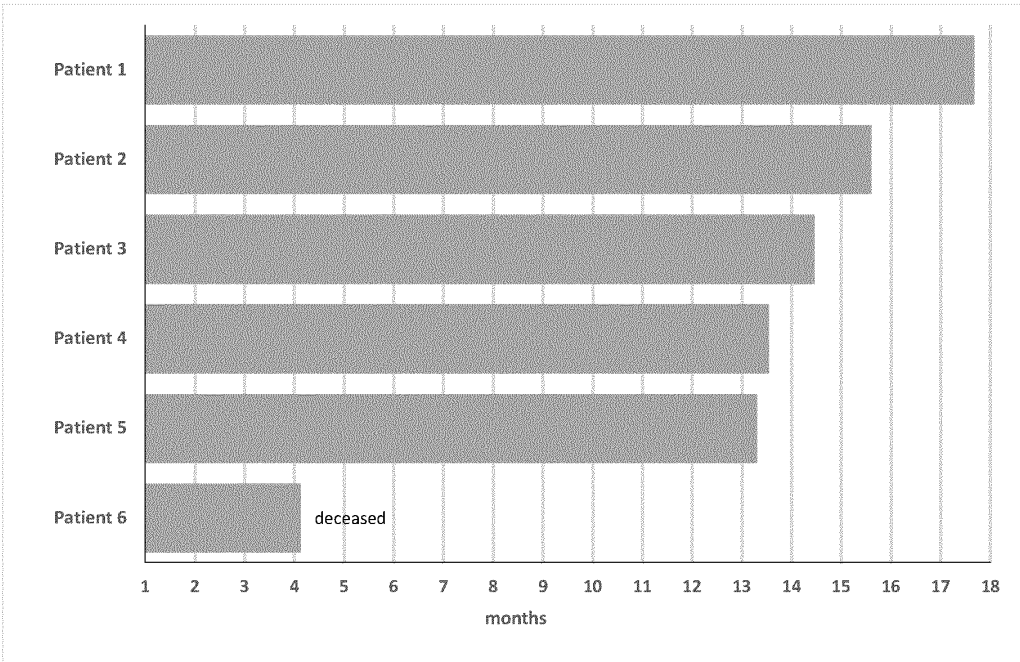


Fig. 28

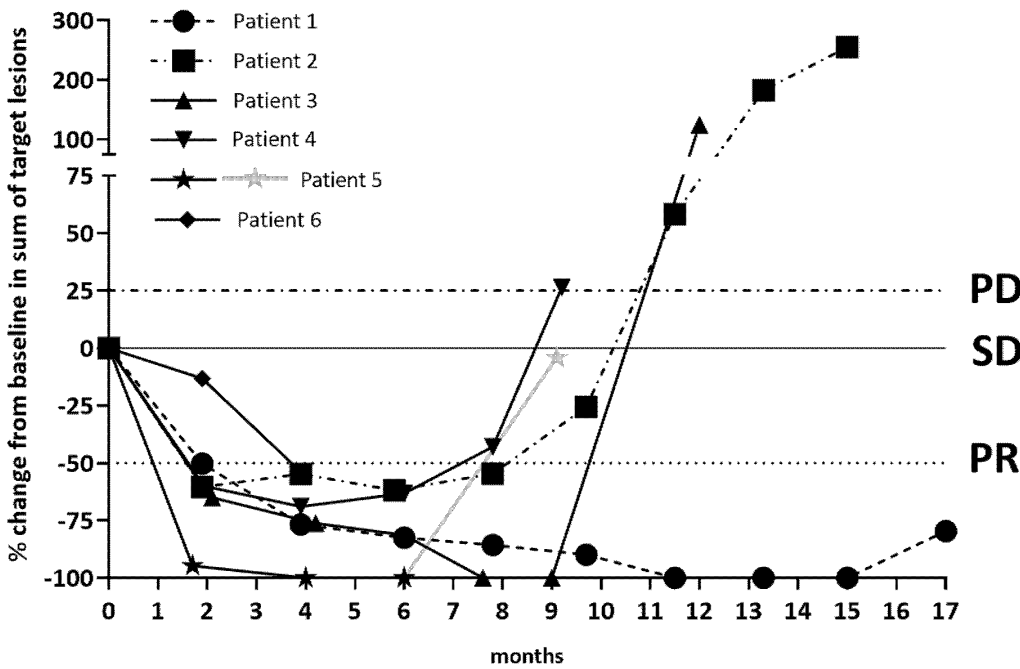


Fig. 29