

Figure 1

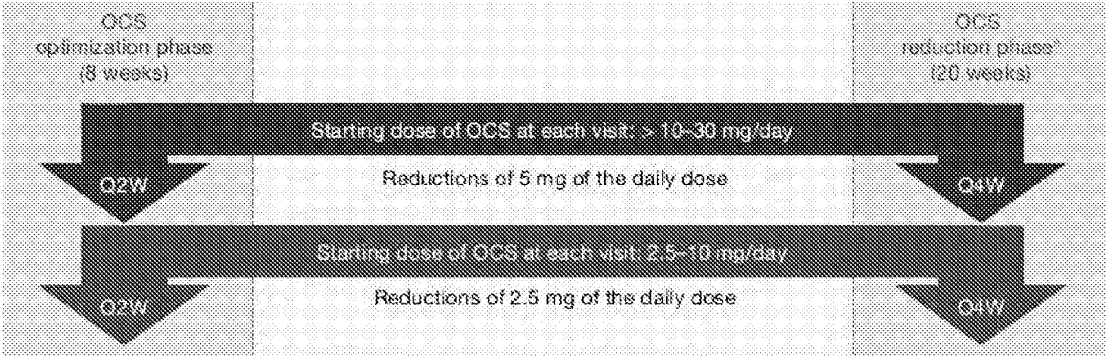


Figure 2A

Asthma Therapy	Total Daily Dose (µg/day)
Inhaled Corticosteroid	High
Beclomethasone dipropionate (pMDI, standard particle HFA)	> 1000
Beclomethasone dipropionate (pMDI or DPI extrafine particle, HFA)	> 400
Ciclesonide (pMDI, extrafine particle, HFA)	> 320
Fluticasone furoate (DPI) eg. Arnuity® Ellipta®	200
Fluticasone propionate (DPI, or pMDI, standard particle, HFA)	> 500
Budesonide (DPI, or pMDI, standard particle HFA)	> 800
Mometasone furoate (pMDI, standard particle, HFA)	> 440
Mometasone furoate (DPI)	Depends on DPI device- see product information
Inhaled Corticosteroid in ICS/LABA combination^a	High
Beclomethasone dipropionate (eg, Fostair®)	> 400
Fluticasone propionate HFA (eg, Seretide®, Advair®)	> 500
Fluticasone furoate (eg, Relvar® Ellipta®, Breo® Ellipta®)	184 - 200
Budesonide, if as delivered dose (eg, Symbicort®)	> 640
Mometasone Furoate (eg, Dulera®)	> 400

^a The ICS doses for the ICS/LABA combinations were derived from GINA 2022 and using prescribing information.

Figure 2B

Asthma therapy (adults and adolescents 12 years and older)	Total daily dose (µg/day) ^b	
Inhaled corticosteroid ^a	Medium	High
Beclomethasone dipropionate CFC ^c	> 500 - 1000	> 1000
Beclomethasone dipropionate HFA	> 200 - 400	> 400
Budesonide DPI	> 400 - 800	> 800
Ciclesonide HFA	> 160 - 320	> 320
Flunisolide ^d	2000	> 2000
Fluticasone furoate DPI (eg, Arnuity [®] Ellipta [®]) ^d	n.a.	200
Fluticasone propionate DPI	> 250 - 500	> 500
Fluticasone propionate HFA	> 250-500	> 500
Mometasone furoate	> 220 - 440	> 440
Triamcinolone acetonide	> 1000 - 2000	> 2000
Inhaled corticosteroid in ICS/LABA combination ^d	Medium	High
Beclomethasone dipropionate (eg, Fostair [®])	400	> 400
Fluticasone furoate (eg, Relvar [®] Ellipta, Breo [®] Ellipta)	n.a.	184,200
Fluticasone propionate HFA (eg, Seretide [®] , Advair [®])	> 320 - 460	> 460
Fluticasone propionate DPI (eg, Seretide Diskus [®] , Advair [®] Diskus [®])	> 250 - 500	> 500
Budesonide HFA (eg, Symbicort [®])	320 to < 640	640
Budesonide DPI (eg, Symbicort Turbuhaler [®])	400 to <800	800
Mometasone furoate HFA (eg, Dulera [®])	400	800
Mometasone DPI (eg, Asmanex [®] Twisthaler [®])	330 – 440	> 440
Abbreviations: CFC = chlorofluorocarbon propellant; DPI = dry powder inhaler; HFA = hydrofluoroalkane propellant; ICS = inhaled corticosteroid; LABA = long-acting β-agonist; n.a. = not applicable a. Modified from the Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma (GINA) 2018. Available from: http://ginaasthma.org/2018-gina-report-global-strategy-for-asthma-management-and-prevention. b. This protocol also allows any product with clinically comparable doses, including newer products and authorised generics. High-dose ICS via nebulised solution for inhalation is also allowed. For products not listed in this table, the highest approved maintenance ICS or ICS/LABA dose in the local country label will meet the protocol-defined criterion for "high-dose ICS." See Section 5.1. Additionally, in countries where the high-dose ICS or ICS/LABA is not available (eg, only the medium-dose ICS or ICS/LABA is available in that country), the highest approved maintenance dose in the local label will also meet this ICS criterion. c. Beclomethasone dipropionate CFC is included for comparison with older literature. d. See local label. Note: Data provided from GINA 2018 is not a table of equivalence, but of estimated clinical comparability. Categories of "low," "medium," and "high" doses are based on published information and available studies (at the time of GINA 2018 publication), including direct comparisons where available. Doses may be country-specific depending on labelling requirements. Most of the clinical benefit from ICS is seen at low doses, and clear evidence of dose-response relationships is seldom available within the dose ranges evaluated for regulatory purposes. "High" doses are arbitrary, but for most ICS are those that, with prolonged use, are associated with increased risk of systemic side-effects. For new preparations, manufacturer's information should be reviewed carefully; products containing the same molecule may not be clinical equivalent (GINA 2018).		

Figure 2C

Oral Corticosteroid	Approximate equivalence dose
Prednisone	10 mg
Prednisolone	10 mg
Cortisone	50 mg
Hydrocortisone	40 mg
Methylprednisolone	8 mg
Triamcinolone	8 mg
Betamethasone	1.2 mg
Dexamethasone	1.5 mg
Deflazacort	12 mg

Figure 3

	NAVIGATOR (n = 42)		SOURCE (n = 92)	
	Tezepelumab only (n = 29)	Placebo only (n = 13)	Tezepelumab only (n = 60)	Placebo only (n = 32)
100% reduction in daily OCS dose by week 48 while maintaining asthma control, ^a n (%)	N/A ^b	N/A ^b	37 (61.7)	17 (53.1)
100% reduction in daily OCS dose by week 154 while maintaining asthma control, n (%)	11 (37.9)	1 (7.7)	40 (66.7)	15 (46.9)

Figure 4

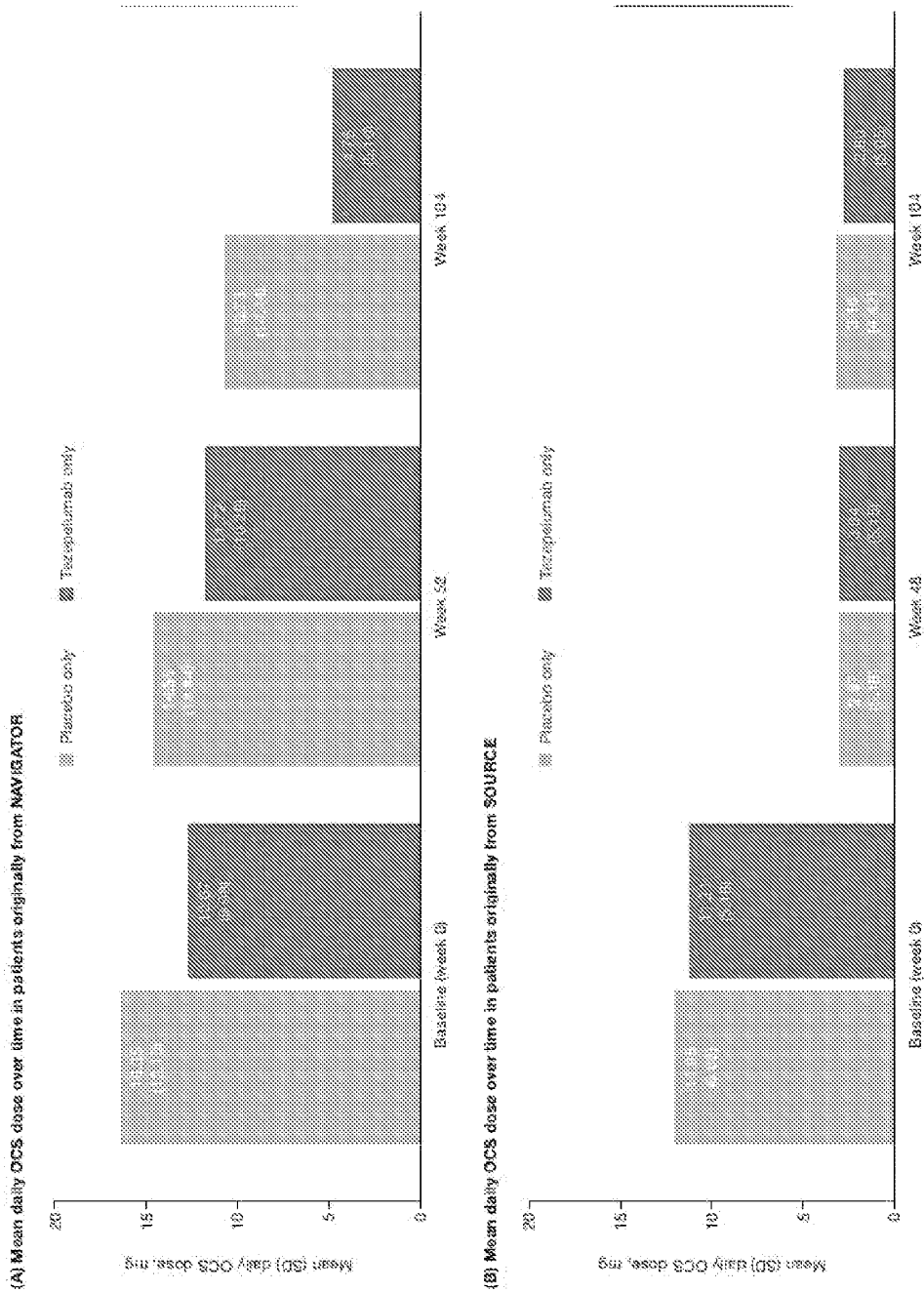


Figure 5

SEQ ID NO	Description	Sequence
1	TSLP nucleotide seq	gcagccagaaagctctggagcatcaggggagactccaacttaaggcaacagcatgggtgaataagggtctcctgtgactggcaatgagaggcaaaaacctgggtgcttgagcactggccctaaagcaggcccttacagatctcttactactcgtgggtggaagagtttagtgtaaaactgggtggaattgggtgtccacgtatgttcccttttgccttactatatgtctgtcagttcttccaggaaaaacttccatcttcaactttagggctggtgttaacttaacgttcaactaactgtgactttgagaagattaaagcagcctatctcagtaactatttctaaagcctgattacatatatgagtgggaccaaagtacogagttcaacaaacacccgtctctttagcaatcgccacattgccttactgaaatccagagcctaacctcaatcccacccggctgcgtgcgtcgccaaagaaatgttcgccaatgaaaactaagggtgccttagctatctgggtcccaggctattcggaactcagataaaatgactactcaggcaatgaagaggagagaaaaaggaaagtcaacaaccaataaattgtctggacaagtgtcacaattacaaggatttggcgctcgcttcaatcgacaccttactgaaacaacagtaaacaccatctttattatggtcatatttccacagccccaaaaataaatcatctttattaaagtaaaaaaaa aaa
2	TSLP amino acid seq	MFPEALLVLSVSRKIFILQLVGLVLTYYDFTNCDFEIKAAAYLSTISKDLITYMSGTKSTEFNNTVSCSNRPHCLTEIQSLTFENPTAGCASLAKEMFAMTKAALAIWCPGSETQINATQAMKKRRKRKVITNKCLEQVSQLOQLWRRFNRLLLKQQ
3	Light chain CDR1	GGNLLGSKSVH
4	Light chain CDR2	DDSDRPS
5	Light chain CDR3	QVWDSSSDHVV
6	Heavy chain CDR1	TYGMH
7	Heavy chain CDR2	VIWYDGSNKHYSVKG
8	Heavy chain CDR3	APQWELVHEAFDI
9	VH nucleotide	cagatgcagctggtgagctctggggaggcgtgggtccagcctgggaggtccctgagactctcctgtgcagcgtctggattcaccttcagaaactatggcatgcactgggtccgcccaggtccaggaaggactggagtgggtggcagttatatggtatgatggaagtaataaacactatgcagactccgtgaaggccgattccaccatcacccagagacaaatccaagaacactctgaaatctgcaaatgaacacgacctgagaccgagcacacgctgtgttactactgtgcgagagccctcagtgggagctagttcatgaagcttttgatatctcggggccaaaggacaaatggtcacccgtctcttcaGGNNLGSKSVHDDSDRPSQVWDSSSDHVVTYGMHVIWYDGSNKHYSVKGAPQWELVHEAFDIQWLVSQGGVVQGRSLRLSCAASGFTFRTYGMHWVRQAPGKGLEWVAVIWYDGSNKHYSVKGKRFITTRDNSKNTLNLQMN SLRAEDTAVYYCARAPQWELVHEAFDIWGQGTMTVSS
10	VH amino acid	

11	VL nucleotide	tcctatgtgtgactcagccaccctcgggtcagtggtgccccaggaagacagccaggtaccctgtggtggggaagaa caaccttggaagtataaagtgtgcaatggtaccagcagagccagccagccctgtgctgtctatgatg atagcgaccgcccctcatggtccctgagcgttctctggtctcgaactctgggaacacgcccaccctgaccatc agcagggggaagccggggtatgagccgactattactgtcaggtgtgggatagtagtagtgcatactgtggtatt tcggcgaggagaccacgaactgacctccta
12	VL amino acid	SYVLTPPPSVAPGQTARITCGGNLGSKVHWYQQKPGAPVLVYDDSDRPSWIPERFSGNSGNTAII SRGEAGDEADYCYQVWDSSDHVVEGGTKLTVL
13	Full length heavy, CDRs underlined	QMQLVESGGG <u>VVQGRSIRL</u> <u>SCAASGFTFR</u> <u>TYGMHWVRQA</u> <u>PKGLEWVAV</u> <u>IWYDGSNKHY</u> ADSVKGRFTI <u>TRDNSKNTLN</u> <u>LQMSLRAED</u> <u>TAVYYCARAP</u> <u>QWELVHEAFD</u> <u>IWGQTMVTV</u> SSASTKGPSV <u>FPLAPCSRST</u> <u>SESTAALGCL</u> <u>VKDYFPEPVT</u> <u>VSWNSGALTS</u> <u>GVHTEPAVLQ</u> SSGLYSLSV <u>VTVPSSNFGT</u> <u>QTYTCNVDHK</u> <u>PSNTKVDKTV</u> <u>ERKCCVECPP</u> <u>CPAPPVAGPS</u> VFLPPKPKD <u>TLMISRTPEV</u> <u>TCVVVDVSHE</u> <u>DPEVQFNWYV</u> <u>DGVEVHNAKT</u> <u>KPREEQFNST</u> ERVVSVLTIV <u>HQDWLNGKEY</u> <u>KCKVSNKGLP</u> <u>APIEKTISK</u> <u>KGQPREPQVY</u> <u>TLPPSREEMT</u> KNQVSLTCLV <u>KGFPYSDIAV</u> <u>EWESNGQPEN</u> <u>NYKTTTPMMLD</u> <u>SDGSFFLYSK</u> <u>LTVDKSRWQQ</u> GNVFSCSVMH <u>EALHNHYTQK</u> <u>SLSLSPGK</u>
14	Full length light, CDRs underlined	SYVLTPPPSV <u>SVAPGQTARI</u> <u>TCGGNNLGSK</u> <u>SVHWYQQKPG</u> <u>QAPVLVYVDD</u> <u>SDRPSWIPER</u> FSGNSGNIA <u>TLTISRGEAG</u> <u>DEADYQCQVW</u> <u>DSSSDHVVFG</u> <u>GGTKLTVLQG</u> <u>PKAAPSVTLF</u> PPSSEELQAN <u>KATLVCLISD</u> <u>FYPGAVTVAW</u> <u>KADSSPVKAG</u> <u>VETTTTPSKQS</u> <u>NNKYAASSYL</u> SLTPEQWKSH <u>RSYSCQVTHE</u> <u>GSTVEKTVAP</u> <u>TECS</u>

Figure 5 continued

Figure 6

Initial OCS dose/day	OCS down-titration to reach an OCS dose of:				
	20 mg	10 mg	7.5 mg	5 mg	0 mg
> 20 mg	Reduction of 5 mg of the daily dose weekly until reaching dose of 20 mg/day	Reduction of 5 mg of the daily dose Q2W until reaching dose of 10 mg/day	2.5 mg of the daily dose Q2W until reaching dose of 7.5 mg/day	2.5 mg of the daily dose Q4W until reaching dose of 5 mg/day	No AI: reductions of 2.5 mg of the daily dose Q4W until reaching dose of 0 mg/day Partial AI: reductions of 1 mg of the daily dose Q4W and repeat test 2 months later ^b Complete AI: No OCS dose reduction and repeat test 3 months later ^b
> 10 mg to ≤ 20 mg		Reduction of 5 mg of the daily dose Q2W until reaching dose of 10 mg/day	2.5 mg of the daily dose Q2W until reaching dose of 7.5 mg/day	2.5 mg of the daily dose Q4W until reaching dose of 5 mg/day	No AI: reductions of 2.5 mg of the daily dose Q4W until reaching dose of 0 mg/day Partial AI: reductions of 1 mg of the daily dose Q4W and repeat test 2 months later ^b Complete AI: No OCS dose reduction and repeat test 3 months later ^b
> 7.5 mg to ≤ 10 mg			2.5 mg of the daily dose Q2W until reaching dose of 7.5 mg/day	2.5 mg of the daily dose Q4W until reaching dose of 5 mg/day	No AI: reductions of 2.5 mg of the daily dose Q4W until reaching dose of 0 mg/day Partial AI: reductions of 1 mg of the daily dose Q4W and repeat test 2 months later ^b Complete AI: No OCS dose reduction and repeat test 3 months later ^b
> 5 mg to ≤ 7.5 mg				2.5 mg of the daily dose Q4W until reaching dose of 5 mg/day	No AI: reductions of 2.5 mg of the daily dose Q4W until reaching dose of 0 mg/day Partial AI: reductions of 1 mg of the daily dose Q4W and repeat test 2 months later ^b Complete AI: No OCS dose reduction and repeat test 3 months later ^b
5 mg					No AI: reductions of 2.5 mg of the daily dose Q4W until reaching dose of 0 mg/day Partial AI: reductions of 1 mg of the daily dose Q4W and repeat test 2 months later ^b Complete AI: No OCS dose reduction and repeat test 3 months later ^b

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^aPartial AI cortisol testing confirmed with ACTH stimulation testing or the alternative method described in Appendix M. After repetition of the test 2 months later, the decision to further reduce OCS dose will be based on the morning cortisol test results. If test results are normal, the OCS dose may be reduced directly to 0 mg/day (if participant is receiving ≤ 3 mg); the participant will continue receiving 1 mg Q4W if still at risk. If complete AI is indicated, OCS dose will not be modified.

^b If morning cortisol test results again indicate complete AI at 3 months, the OCS dose will not be modified as this is the final attempt. If morning cortisol test results indicate risk AI, then reductions will be 1 mg Q4W and, if normal, then reductions will be 2.5 mg Q4W.

Figure 7A

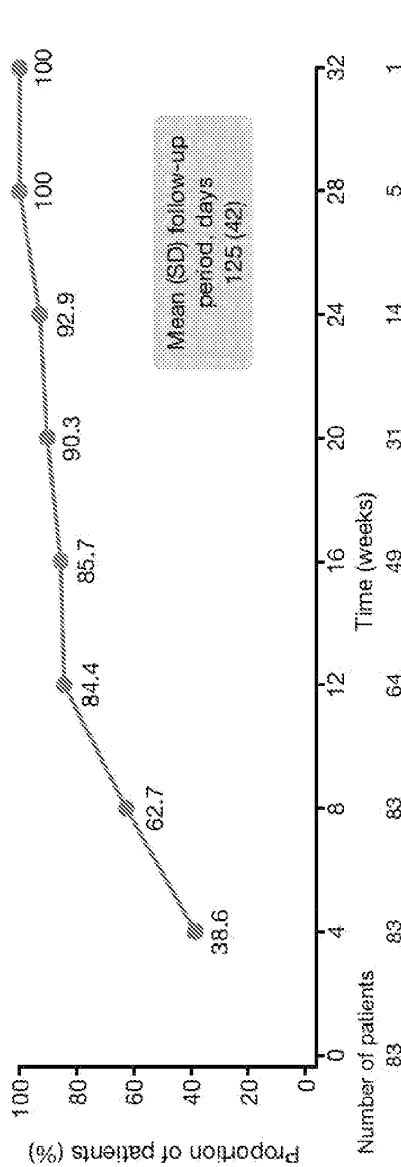


Figure 7B

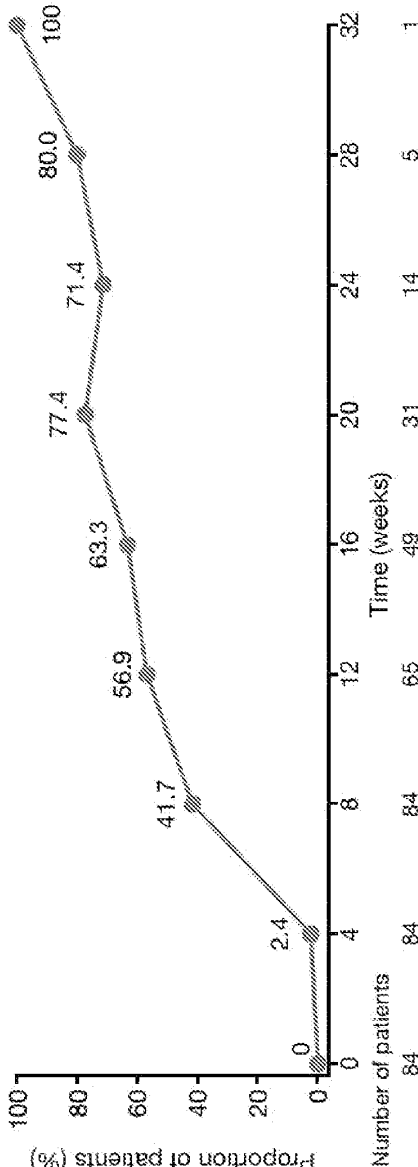


Figure 8

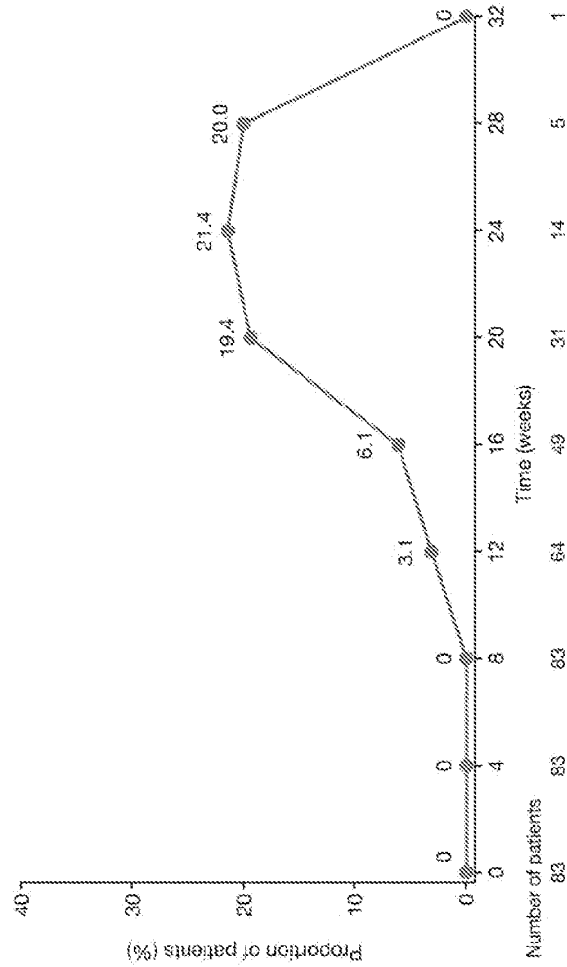


Figure 9A

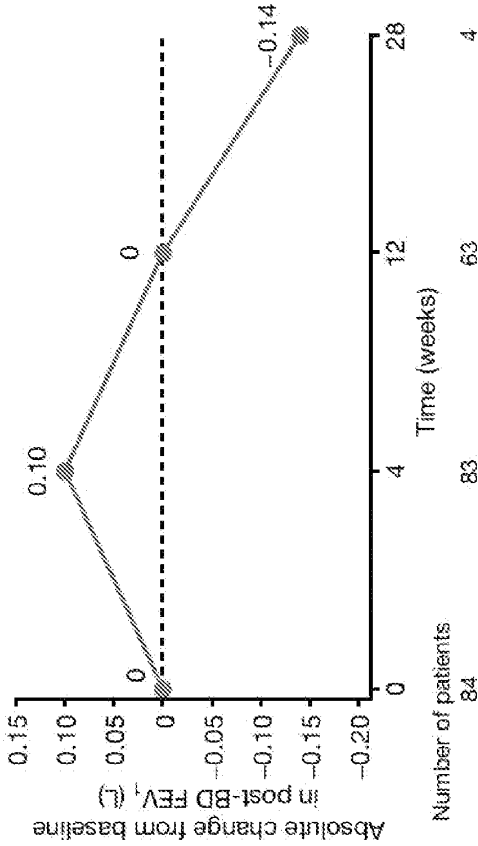


Figure 9B

