

[Fig. 1]

High Level Summary of Trials

Design	Dose QD XR	Endpoints
6-week, DB, PC Ages 13-17y	164.4 mg* 328.8 mg* Placebo	ADHD RS-5 CGI-S Conners-3 Parent Short content scales: Hyperactivity-Impulsivity, Inattention, Defiance/aggression, and Executive Functioning
6-week, DB, PC Ages 6-12y***	Low dose*** High dose*** Placebo	ADHD RS-5 CGI-S Conners-3 Parent Short content scales: Hyperactivity-Impulsivity, Inattention, Defiance/aggression, and Executive Functioning

* Equivalent to 200 and 400 mg total daily doses in SR formulation used in adults; **weight-based dosing for ages 6-12y; DB = double blind; PC = placebo controlled

FIGURE 1

[Fig. 2]

Trial Designs (Adolescents and Children)

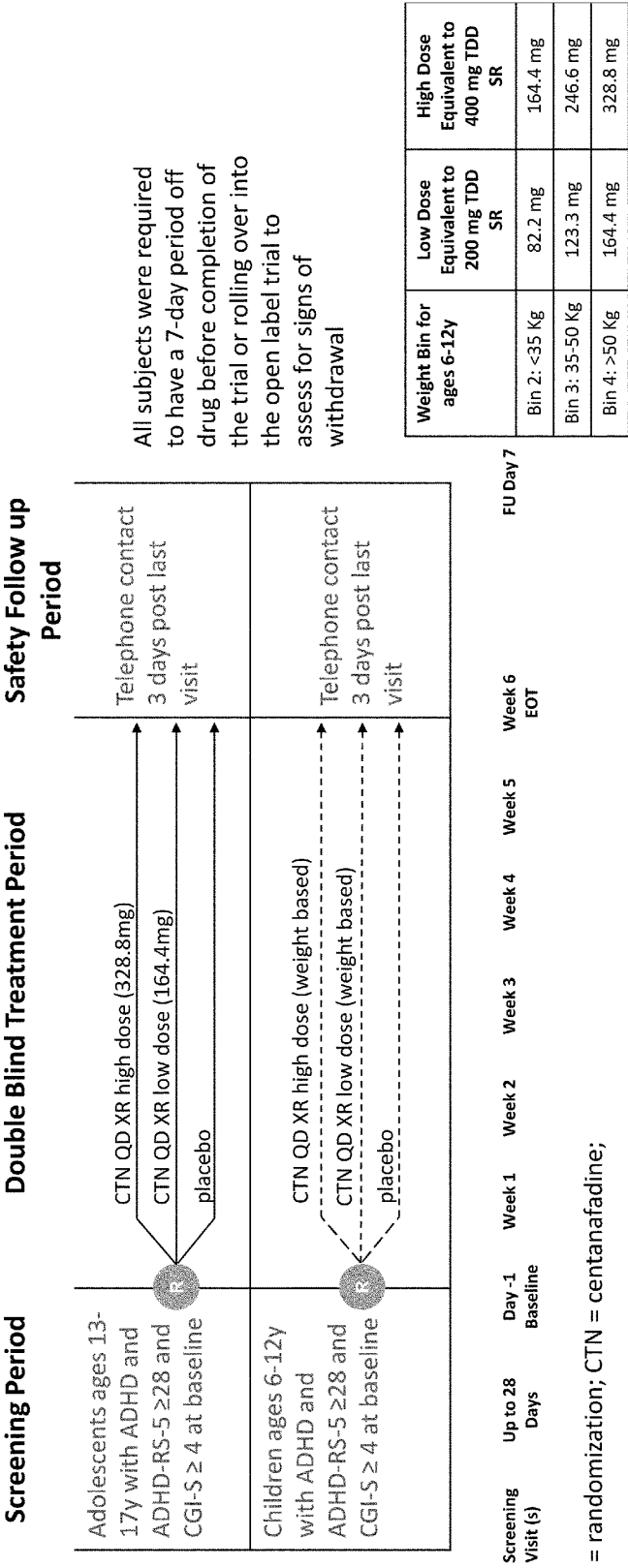


FIGURE 2

R = randomization; CTN = centanafadine;

[Fig. 3]

Key Inclusion / Exclusion Criteria

- Inclusion Criteria
 - Primary diagnosis of ADHD based on the DSM-5 diagnosis criteria and confirmed with the MINI-KID
 - A minimum symptoms total raw score of ≥ 28 on the ADHD-RS-5 at baseline
 - A score of ≥ 4 on the CGI-S-ADHD at baseline
- Exclusion Criteria
 - A comorbid diagnosis of: Tourette's Disorder, GAD that is severe enough to interfere with trial procedures, Panic Disorder, Conduct Disorder, Psychosis, PTSD, Bipolar Disorder, ASD, ODD that is severe enough to interfere with trial conduct, OCD that is severe enough to interfere with trial conduct, MDD with current MDE, or has required treatment within the 3 months prior to screening
 - No suitable therapeutic benefit has been derived from adequate courses of 2 classes of therapy for ADHD during the subject's lifetime, in the investigator's opinion

FIGURE 3

[Fig. 4]

Endpoints

Primary Endpoint:

- Change from baseline in the ADHD-RS-5 symptoms total raw score at Week 6

Key Secondary Endpoints:

- Change from baseline in CGI-S-ADHD at Week 6
- Change from baseline in Conners 3 Parent Short t-score at Week 6
 - Hyperactivity/Impulsivity content scale
 - Inattention content scale
 - Defiance/Aggression content scale
 - Executive Functioning content scale

FIGURE 4

[Fig. 5]
CTN = centanafadine; *Only one reason for discontinuation was permitted for each subject.

Subject Disposition Adolescents

	Adolescents (N=459)			
	CTN 164.4 mg (%)	CTN 328.8 mg (%)	Placebo (%)	Total (%)
Randomized	155	155	149	459
Completed	124 (80.0%)	122 (78.7%)	125 (83.9%)	371 (80.8%)
Discontinued*	31 (20.0%)	33 (21.3%)	24 (16.1%)	88 (19.2%)
Adverse Event	5 (3.2%)	12 (7.7%)	0 (0.0%)	17 (3.7%)
Reasons unrelated to medical condition	1 (0.6%)	1 (0.6%)	1 (0.7%)	3 (0.7%)
Lost to Follow up	4 (2.6%)	5 (3.2%)	8 (5.4%)	17 (3.7%)
Site terminated by Sponsor	1 (0.6%)	0 (0.0%)	0 (0.0%)	1 (0.2%)
Lack of efficacy	0 (0.0%)	1 (0.6%)	0 (0.0%)	1 (0.2%)
Non compliance with study drug	2 (1.3%)	0 (0.0%)	1 (0.7%)	3 (0.7%)
Physician Decision	1 (0.6%)	3 (1.9%)	2 (1.3%)	6 (1.3%)
Randomized by mistake	1 (0.6%)	0 (0.0%)	0 (0.0%)	1 (0.2%)
Randomized by mistake with study treatment	0 (0.0%)	0 (0.0%)	2 (1.3%)	2 (0.4%)
Withdrawal by subject	5 (3.2%)	1 (0.6%)	0 (0.0%)	6 (1.3%)
Withdrawal by parent or legal guardian	8 (5.2%)	5 (3.2%)	6 (4.0%)	19 (4.1%)
Withdrawal of informed consent/assent	0 (0.0%)	1 (0.6%)	0 (0.0%)	1 (0.2%)
Other	3 (1.9%)	4 (2.6%)	4 (2.7%)	11 (2.4%)

FIGURE 5

[Fig. 6]

CTN = centanafadine; *Only one reason for discontinuation was permitted for each subject.

Subject Disposition Children

	Children (N=480)			
	CTN low dose (%)	CTN high dose (%)	Placebo (%)	Total (%)
Randomized	154	162	164	480
Completed	118 (76.6%)	124 (76.5%)	125 (76.2%)	367 (76.5%)
Discontinued*	36 (23.4%)	38 (23.5%)	39 (23.8%)	113 (23.5%)
Adverse Event	4 (2.6%)	10 (6.2%)	2 (1.2%)	16 (3.3%)
Lost to Follow up	11 (7.1%)	7 (4.3%)	12 (7.3%)	30 (6.3%)
Site terminated by Sponsor	1 (0.6%)	2 (1.2%)	1 (0.6%)	4 (0.8%)
Lack of efficacy	1 (0.6%)	1 (0.6%)	0 (0.0%)	2 (0.4%)
Noncompliance with study drug	0 (0.0%)	4 (2.5%)	3 (1.8%)	7 (1.5%)
Physician Decision	3 (1.9%)	2 (1.2%)	2 (1.2%)	7 (1.5%)
Randomized by mistake	0 (0.0%)	0 (0.0%)	1 (0.6%)	1 (0.2%)
Randomized by mistake with study treatment	0 (0.0%)	1 (0.6%)	2 (1.2%)	3 (0.6%)
Withdrawal by subject	4 (2.6%)	1 (0.6%)	3 (1.8%)	8 (1.7%)
Withdrawal by parent or legal guardian	10 (6.5%)	8 (4.9%)	12 (7.3%)	30 (6.3%)
Other	2 (1.3%)	2 (1.2%)	1 (0.6%)	5 (1.0%)

FIGURE 6

[Fig. 7]
CTN = centanafadine

Baseline Demographics Adolescents

Event (%)	Adolescents			
	CTN 164.4 mg n=155	CTN 328.8 mg n=155	Placebo n=149	Total n=459
Age (mean in years, min, max)	14.5 (13,17)	14.7 (13,17)	14.7 (13,17)	14.7 (13,17)
Sex at birth - Female n(%)	69 (44.5%)	56 (36.1%)	62 (41.6%)	187 (40.7%)
Weight (mean kg)	65.4	68.9	67.5	67.3
BMI (kg/m ²)	23.7	24.3	24.2	24.1
Race				
White n(%)	106 (68.4%)	110 (71.0%)	107 (71.8%)	323 (70.4%)
Black n(%)	43 (27.7%)	36 (23.2%)	35 (23.5%)	114 (24.8%)
American Indian n(%)	0 (0.0%)	1 (0.6%)	3 (2.0%)	4 (0.9%)
Asian n(%)	4 (2.6%)	1 (0.6%)	1 (0.7%)	6 (1.3%)
Native Hawaiian n(%)	0 (0.0%)	1 (0.6%)	0 (0.0%)	1 (0.2%)
Other n(%)	2 (1.3%)	6 (3.9%)	3 (2.0%)	11 (2.4%)
ADHD-RS-5 Total Score (mean)	37.7	37.8	37.0	37.5
CGI-S-ADHD (mean)	4.5	4.5	4.4	4.5
Conners 3 Parent (mean)				
Hyperactivity/Impulsivity	78.9	80.8	79.8	79.8
Inattention	80.1	81.5	82.2	81.3
Defiance/Aggression	59.5	60.0	57.8	59.3
Executive Function	74.1	74.4	74.5	74.3

FIGURE 7

[Fig. 8]

CTN = centanafadine

Baseline Demographics Children

Event (%)	Children (N=480)			
	CTN low dose n=154	CTN high dose n=162	Placebo n=164	Total n=480
Age (mean in years, min,max)	9.3 (6,12)	9.1 (6,12)	9.2 (6,12)	9.2 (6,12)
Sex at birth - Female n(%)	67 (43.5%)	75 (46.3%)	58 (35.4%)	200 (41.7%)
Weight (mean kg)	41.9	40.8	40.8	41.1
BMI (kg/m ²)	20.4	20.3	19.8	20.1
Race				
White n(%)	102 (66.2%)	105 (64.8%)	105 (64.0%)	312 (65.0%)
Black n(%)	40 (26.0%)	47 (29.0%)	44 (26.8%)	131 (27.3%)
American Indian n(%)	2 (1.3%)	1 (0.6%)	0 (0.0%)	3 (0.6%)
Asian n(%)	1 (0.6%)	2 (1.2%)	2 (1.2%)	5 (1.0%)
Native Hawaiian n(%)	0 (0.0%)	0 (0.0%)	2 (1.2%)	2 (0.4%)
Other n(%)	9 (5.8%)	7 (4.3%)	11 (6.7%)	27 (5.6%)
ADHD-RS-5 Total Score (mean)	43.1	42.9	43.2	43.1
CGI-S-ADHD (mean)	4.9	4.8	4.9	4.8
Conners 3 Parent Short				
Hyperactivity/Impulsivity	84.5	83.5	85.0	84.3
Inattention	84.8	83.1	83.5	83.8
Defiance/Aggression	65.4	64.9	68.2	66.2
Executive Function	78.9	78.1	78.8	78.6

FIGURE 8

Primary Endpoint: LSM Change from Baseline in ADHD-RS-5 Total Raw Score (MMRM) Adolescents

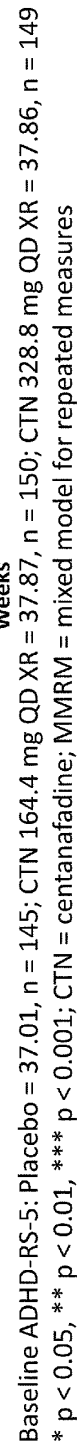
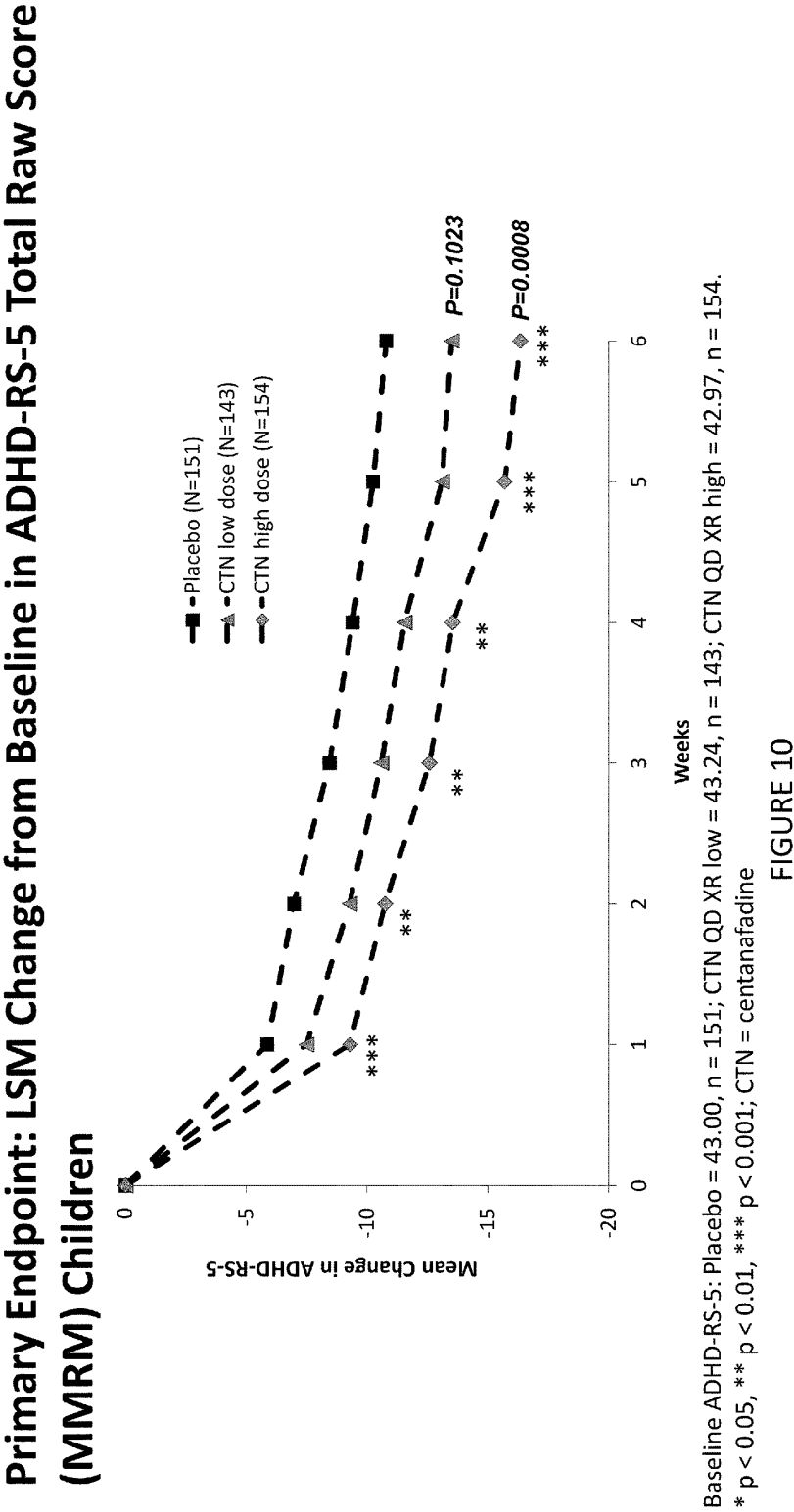


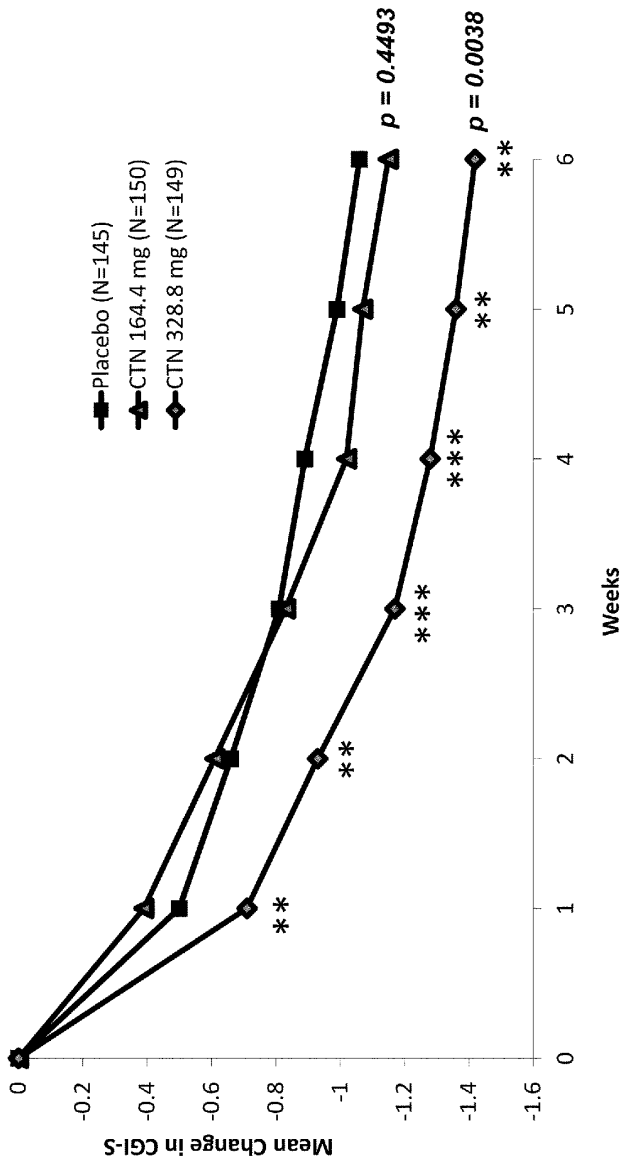
FIGURE 9

[Fig. 10]



[Fig. 11]

Key Secondary: LSM Change from Baseline in CGI-S-ADHD Score (MMRM)
Adolescents

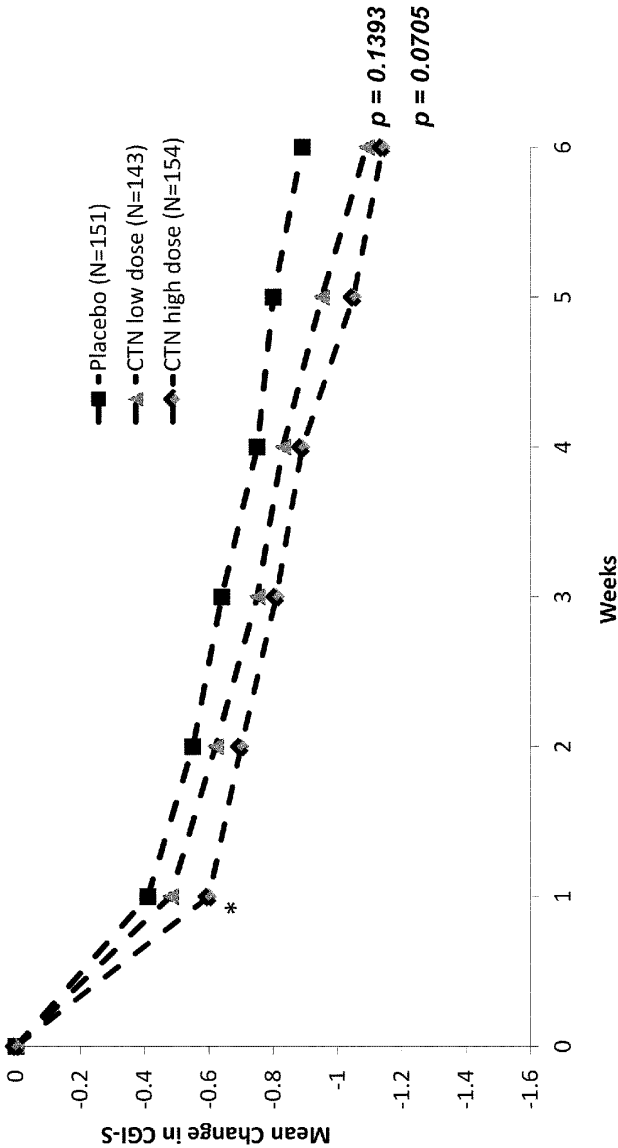


Baseline CGI-S-ADHD: Placebo = 4.43, n = 145; CTN 164.4 mg QD XR = 4.49, n = 150; CTN 328.8 mg QD XR = 4.54, n = 149
** nominal p < 0.01, *** nominal p < 0.001; CTN = centanafadine; LSM = least squares means

FIGURE 11

[Fig. 12]

Key Secondary: LSM Change from Baseline in CGI-S-ADHD Score (MMRM)
Children



Baseline CGI-S-ADHD: Placebo = 4.87, n = 151; CTN QD XR low = 4.87, n = 143; CTN QD XR high = 4.79, n = 154.
* nominal p < 0.05; CTN = centanafadine

FIGURE 12

[Fig. 13]

Dosing Guidance

Weight Bin for ages 6-12y	Low Dose Equivalent to 200 mg TDD SR	High Dose Equivalent to 400 mg TDD SR
Bin 1: <20 Kg	discontinued	discontinued
Bin 2: <35 Kg	82.2 mg	164.4 mg
Bin 3: 35-50 Kg	123.3 mg	246.6 mg
Bin 4: >50 Kg	164.4 mg	328.8 mg

FIGURE 13

[Fig. 14]

Posthoc - Mean Change from Baseline in ADHD-RS-5 Total Raw Score (MMRM)
In Children by Baseline Weight bin

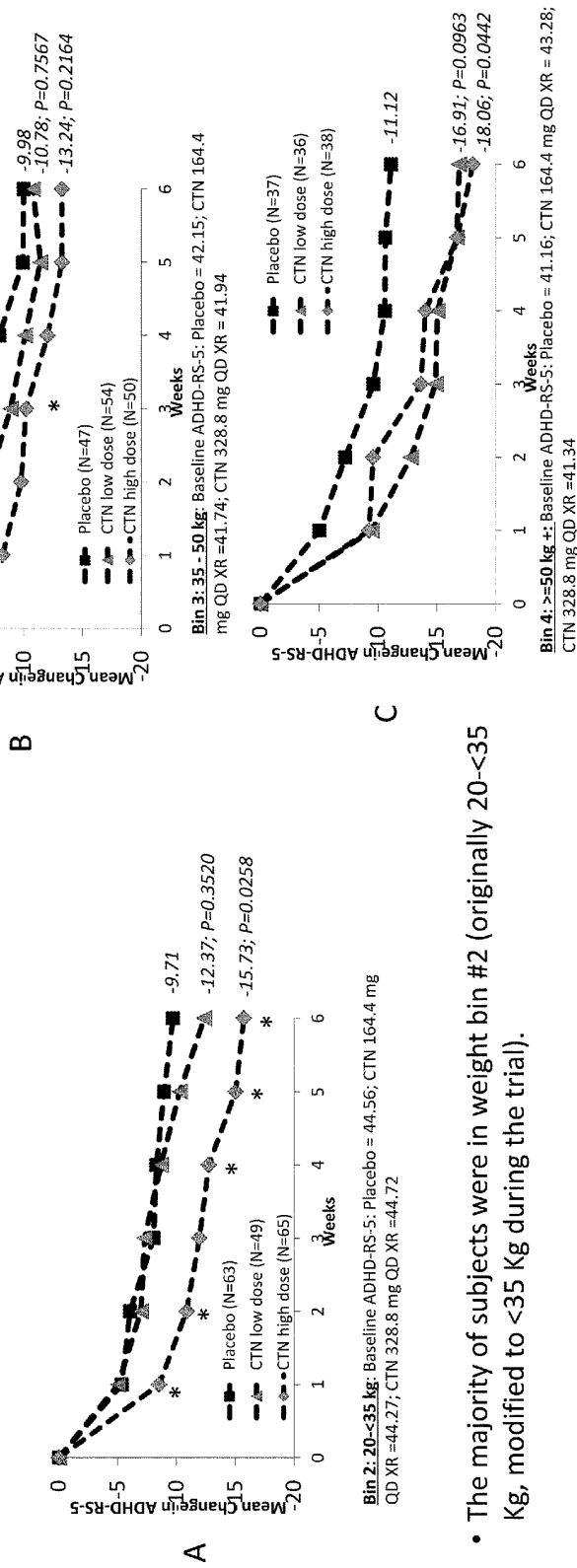


FIGURE 14A-C

- The majority of subjects were in weight bin #2 (originally 20-<35 Kg, modified to <35 Kg during the trial).

[Fig. 15]

Efficacy Conclusions: ADHD-RS-5 and CGI-S Adolescents

- Nominal statistical significance started at Week 1 ($p=0.001$)
- Centanafadine demonstrated a nominally significant difference at Week 6 in the key secondary endpoint of CFB in CGI-S-ADHD vs. placebo for **CTN 328.8 mg (Diff: -0.37; $p=0.0038$)**
- Nominal statistical significance started at Week 1 ($p=0.0085$)

CFB = change from baseline

FIGURE 15

[Fig. 16]

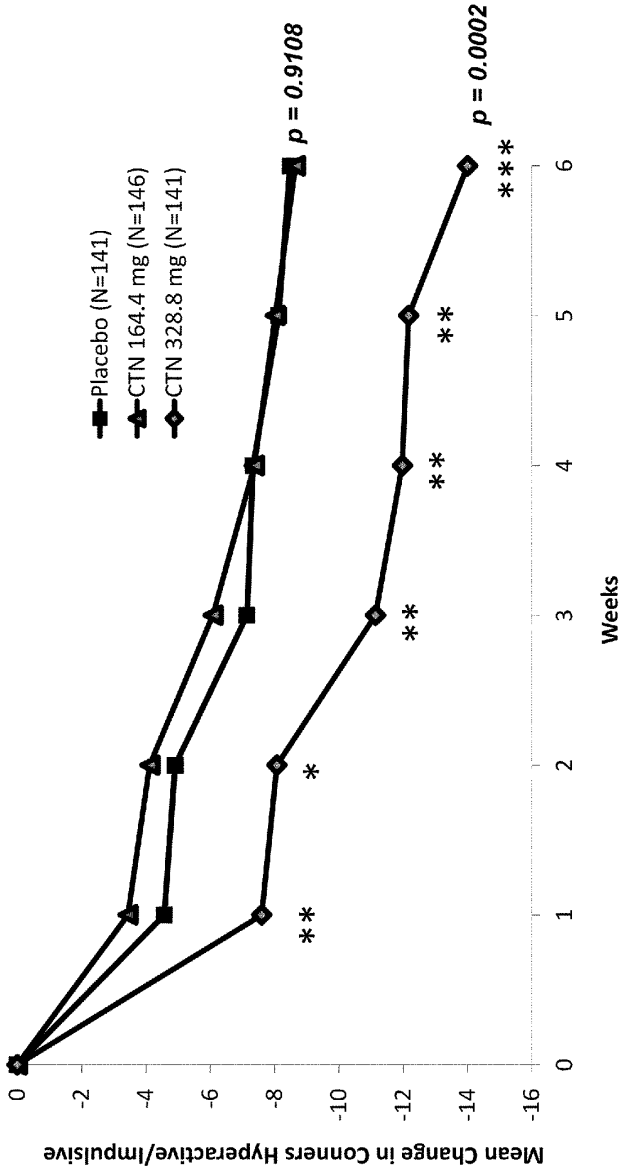
Efficacy Conclusions: ADHD-RS-5 and CGI-S Children

- Nominal statistically significant difference was seen starting at Week 1 ($p=0.0009$)

FIGURE 16

[Fig. 17]

LSM Change from Baseline in Conners-3 Parent Short t-score
Hyperactive/Impulsive Content Scale (MMRM) in Adolescents



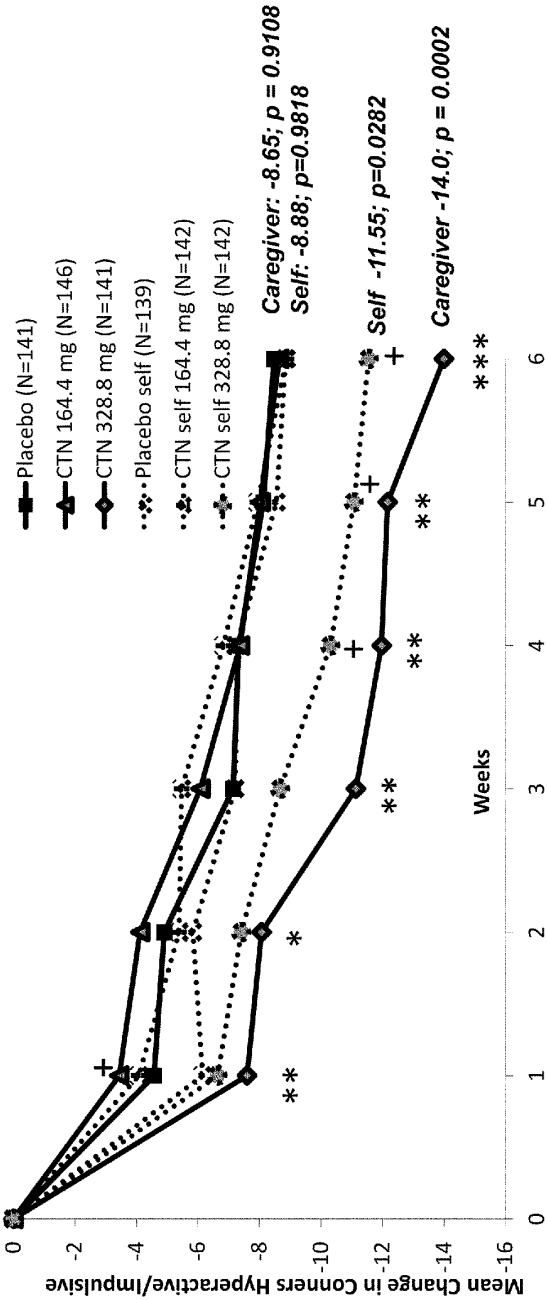
Baseline Hyperactivity/Impulsivity: Placebo = 79.52, n = 141; CTN 164.4 mg QD XR = 78.85, n = 146; CTN 328.8 mg QD XR = 81.42, n = 141.
* nominal $p < 0.05$, ** nominal $p < 0.01$, *** nominal $p < 0.001$; CTN = centanafadine

FIGURE 17

[Fig. 18]

* nominal $p < 0.05$, ** nominal $p < 0.01$, *** nominal $p < 0.001$;
CTN = centanafadine

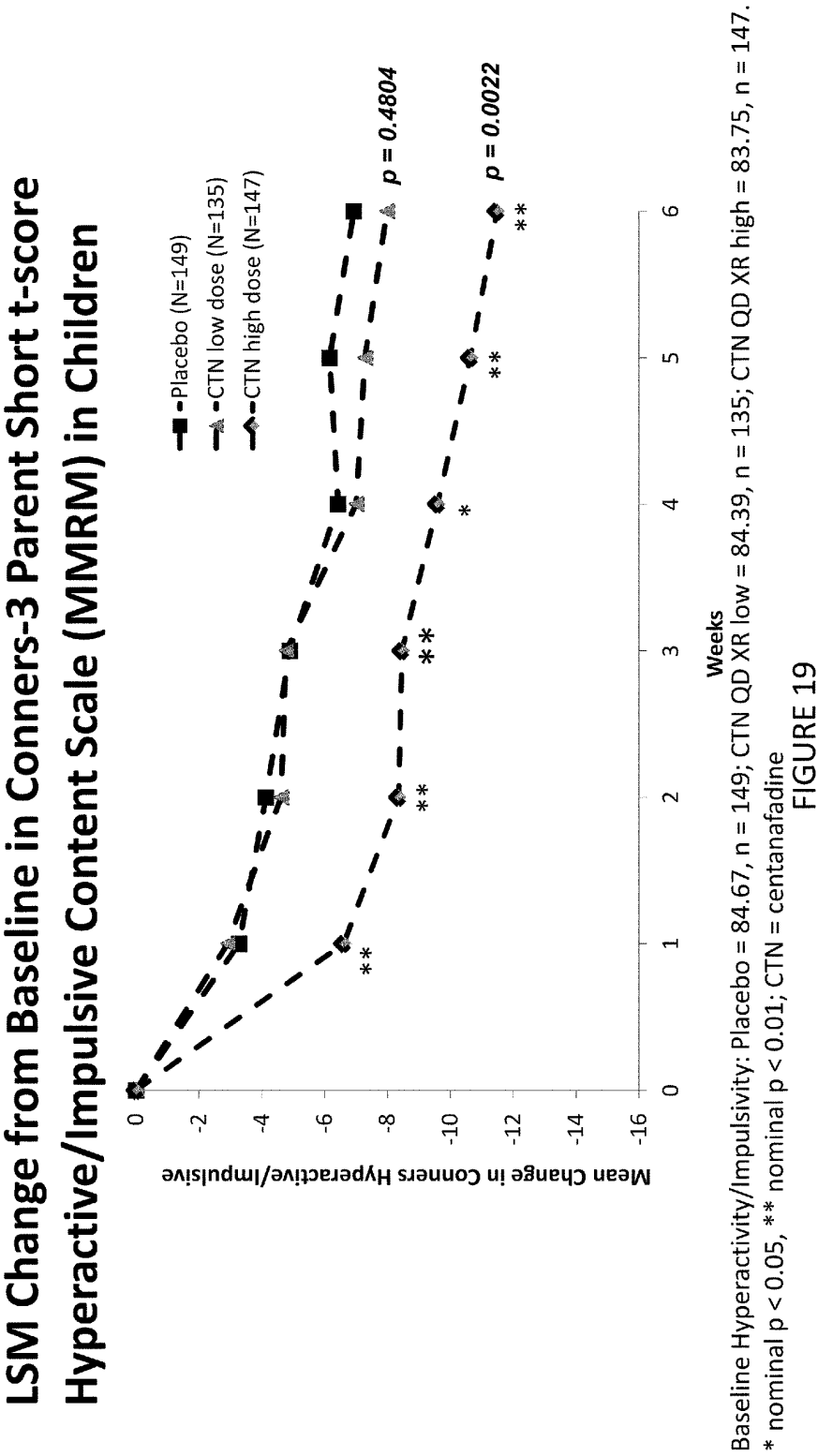
LSM Change from Baseline in Conners-3 Parent Short t-score Hyperactive/Impulsive
Content Scale (MMRM) vs self in Adolescents



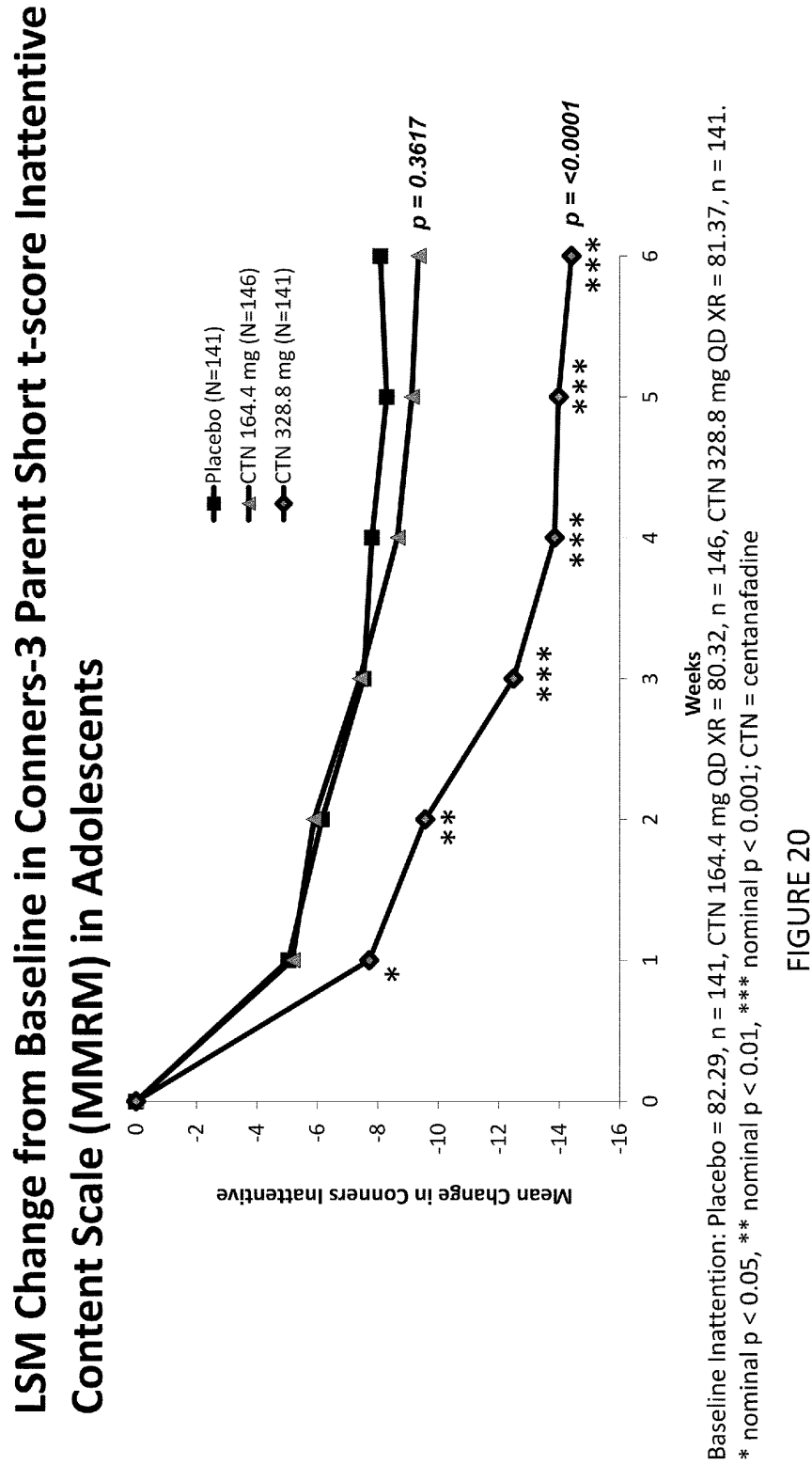
Caregiver: Baseline Hyperactivity/Impulsivity: Placebo = 79.52; CTN 164.4 mg QD XR = 78.85; CTN 328.8 mg QD XR = 81.42.
Self: Baseline Hyperactivity/Impulsivity: Placebo = 69.40; CTN 164.4 mg QD XR = 68.37; CTN 328.8 mg QD XR = 69.53

FIGURE 18

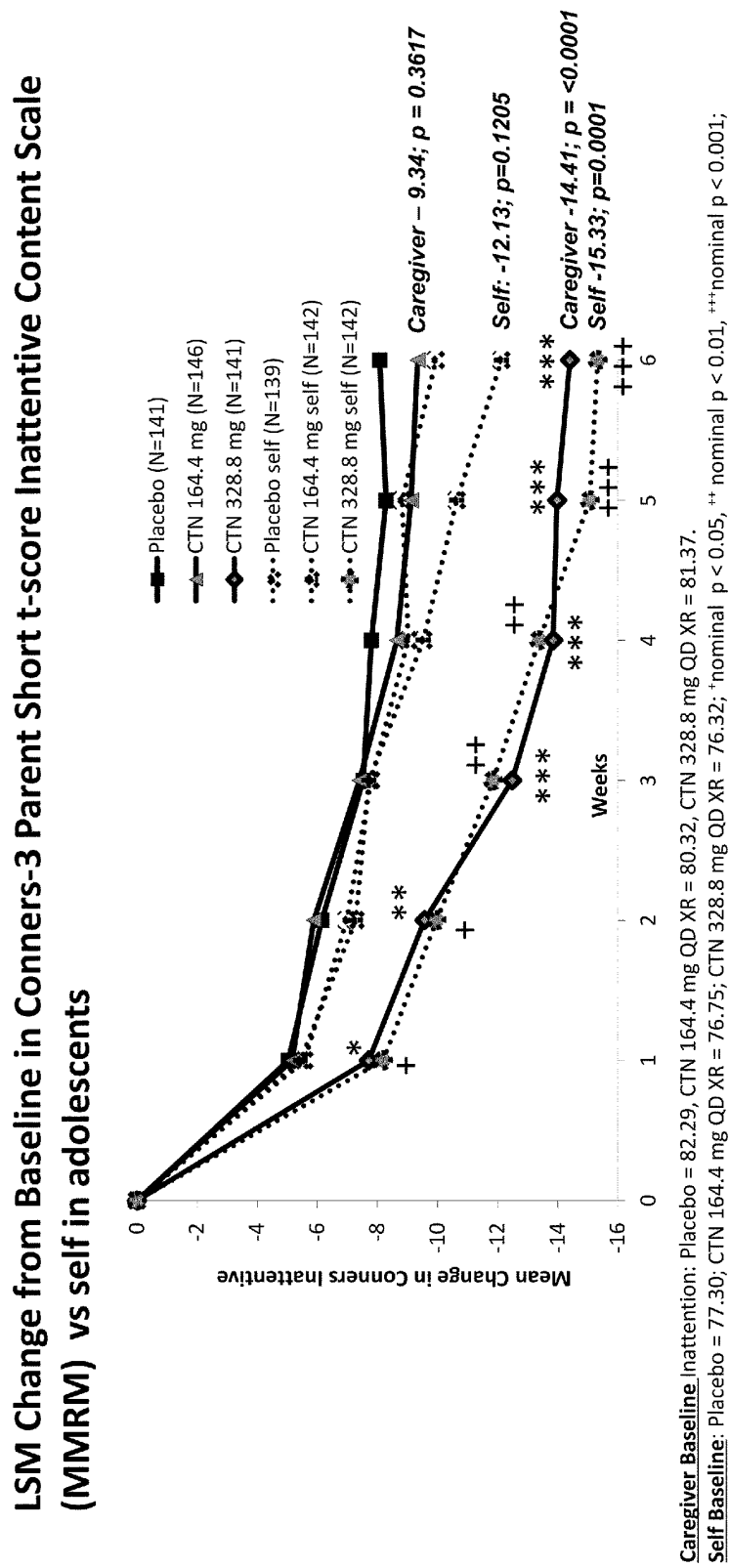
[Fig. 19]



[Fig. 20]

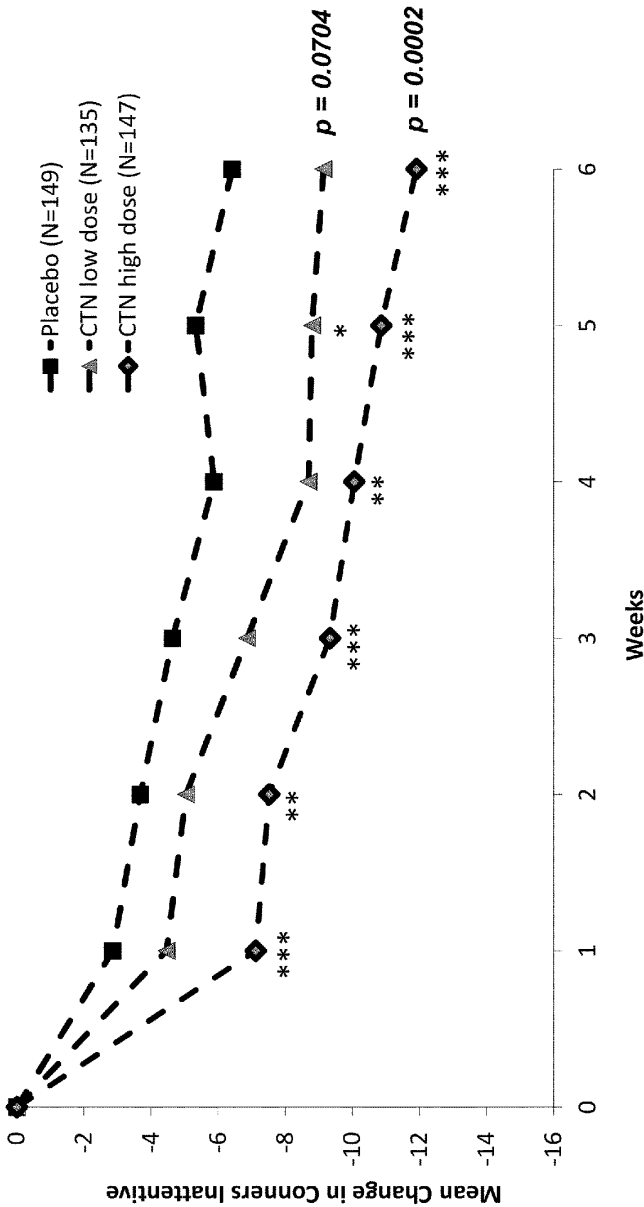


[Fig. 21]



[Fig. 22]

LSM Change from Baseline in Conners-3 Parent Short t-score Inattentive Content Scale (MMRM) in Children

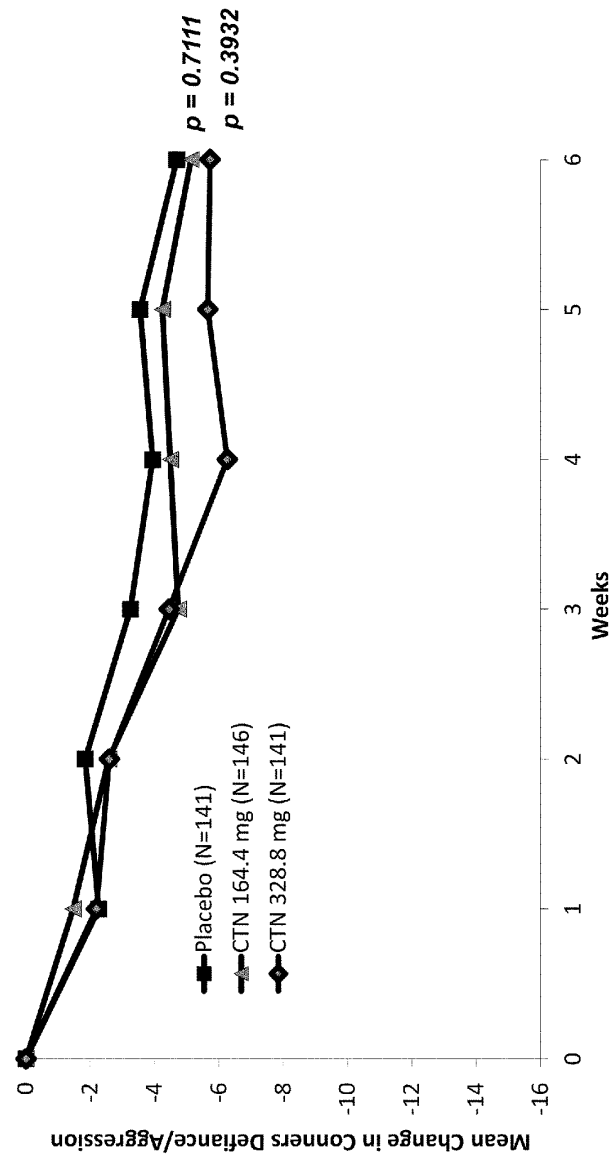


Baseline Inattention: Placebo = 83.30, n = 149, CTN QD XR low = 84.81, n = 135, CTN QD XR high = 83.27, n = 147.
* nominal p < 0.05, ** nominal p < 0.01, *** nominal p < 0.001; CTN = centanafadine

FIGURE 22

[Fig. 23]

LSM Change from Baseline in Conners-3 Parent Short t-score
Defiance/Aggression Content Scale (MMRM) Adolescents



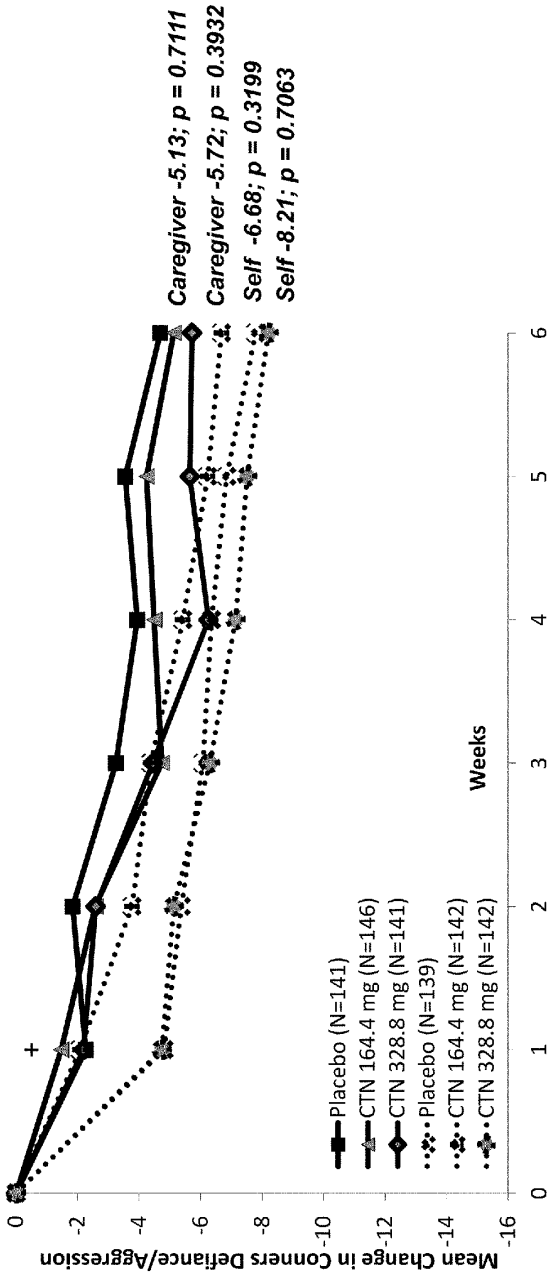
Baseline Defiance/Aggression: Placebo = 57.52, n = 141, CTN 164.4 mg QD XR = 59.41, n = 146, CTN 328.8 mg QD XR = 60.55, n = 141.
CTN = centanafadine

FIGURE 23

[Fig. 24]

CTN = centanafadine

LSM Change from Baseline in Conners-3 Parent Short t-score Defiance/Aggression Content Scale (MMRM) vs self report in adolescents

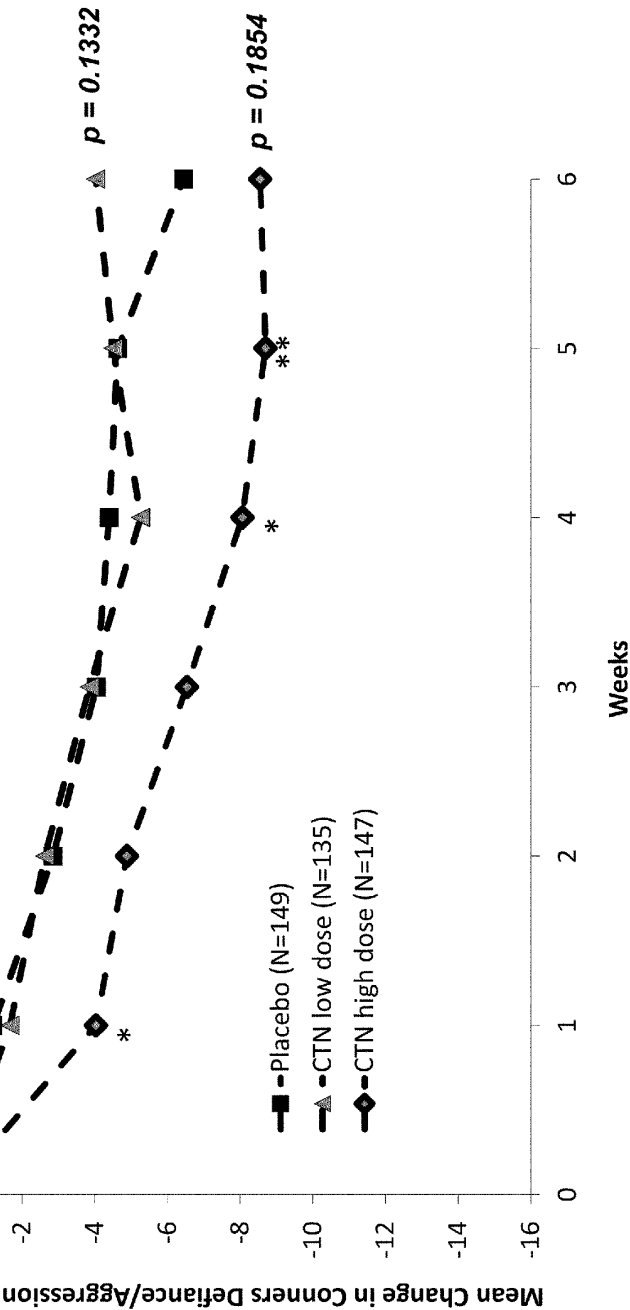


Caregiver Baseline Defiance/Aggression: Placebo = 57.52, CTN 164.4 mg QD XR = 59.41, CTN 328.8 mg QD XR = 60.55.
Self Baseline: Placebo =59.30; CTN 164.4 mg QD XR =56.63; CTN 328.8 mg QD XR =58.33

FIGURE 24

[Fig. 25]

LSM Change from Baseline in Conners-3 Parent Short t-score
Defiance/Aggression Content Scale (MMRM) in Children

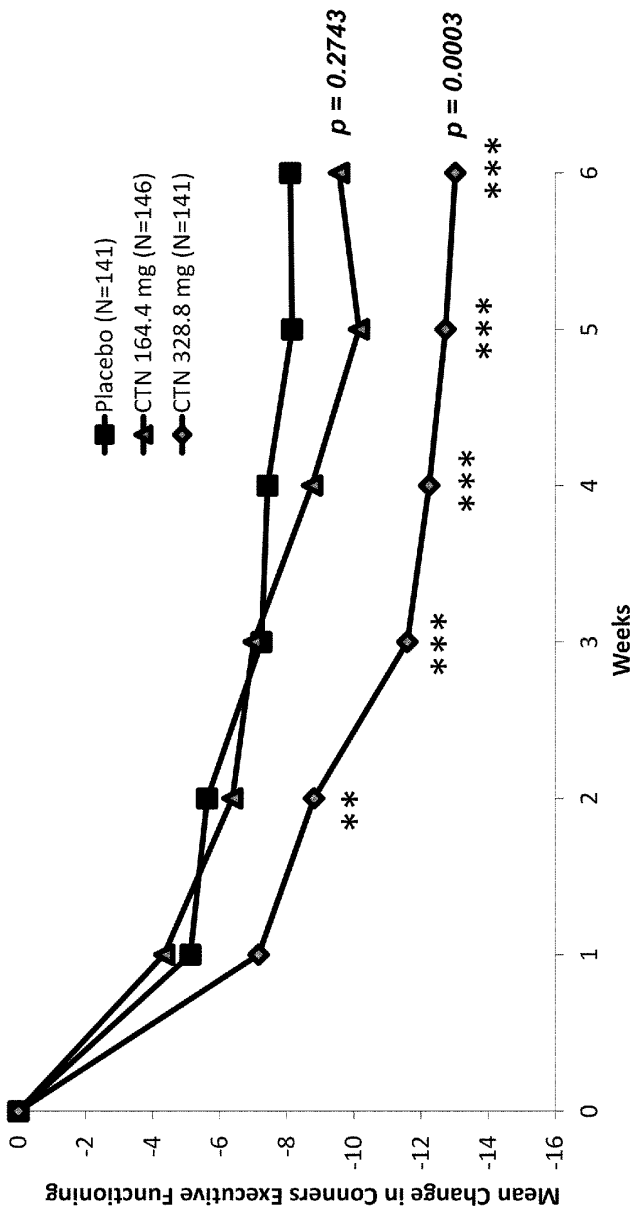


Baseline Defiance/Aggression: Placebo = 67.78, n = 149, CTN QD XR low = 65.59, n = 135, CTN QD XR high = 64.73, n = 147.
* nominal p < 0.05, ** nominal p < 0.01; CTN = centanafadine

FIGURE 25

[Fig. 26]

LSM Change from Baseline in Conners-3 Parent Short t-score Executive Functioning Content Scale (MMRM) in Adolescents

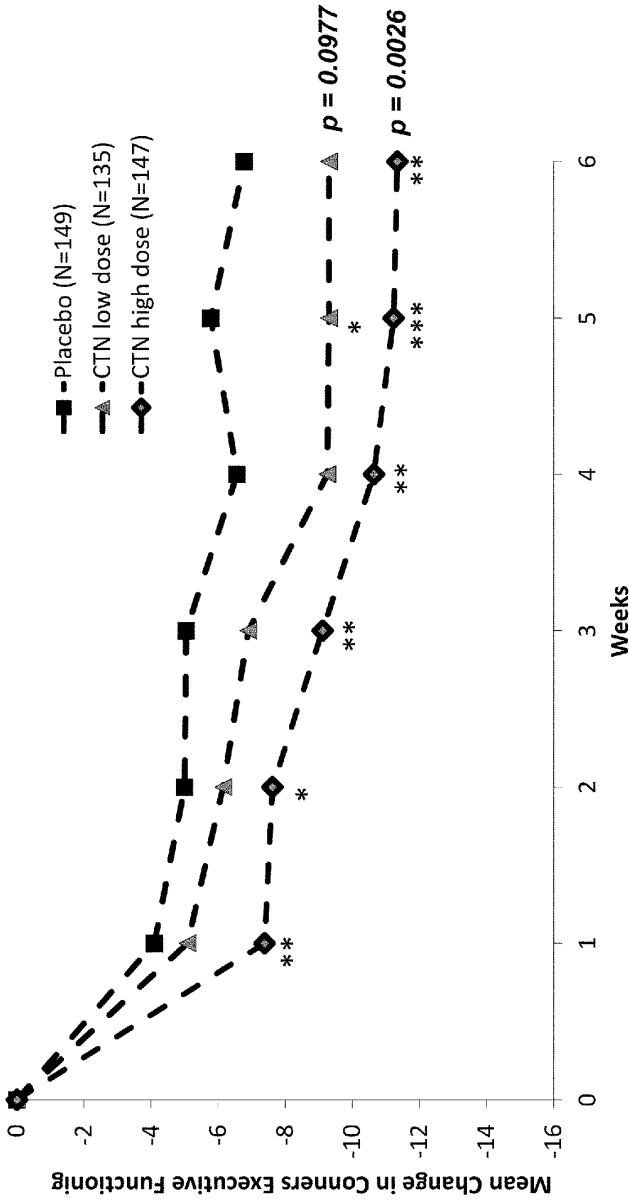


Baseline Executive Function: Placebo = 74.65, n= 141; CTN 164.4 mg QD XR = 74.20, n = 146; CTN 328.8 mg QD XR = 74.50, n = 141.
* nominal p < 0.05, ** nominal p < 0.01, *** nominal p < 0.001; CTN = centanafadine

FIGURE 26

[Fig. 27]

LSM Change from Baseline in Conners-3 Parent Short t-score Executive Functioning Content Scale (MMRM) in Children

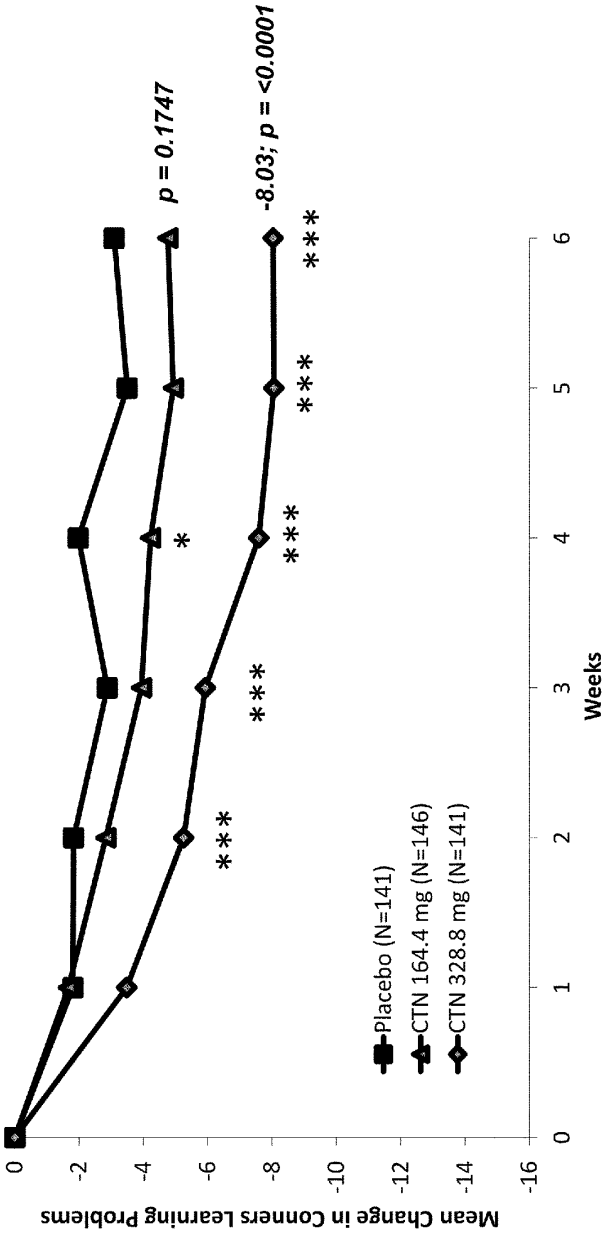


Baseline Executive Function: Placebo = 78.46, n = 149; CTN QD XR low = 79.01, n = 135; CTN QD XR high = 78.44, n = 147
* nominal p < 0.05, ** nominal p < 0.01, *** nominal p < 0.001; CTN = centanafadine

FIGURE 27

[Fig. 28]

LSM Change from Baseline in Conners-3 Parent Short t-score Learning Problems Content Scale (MMRM) in adolescents

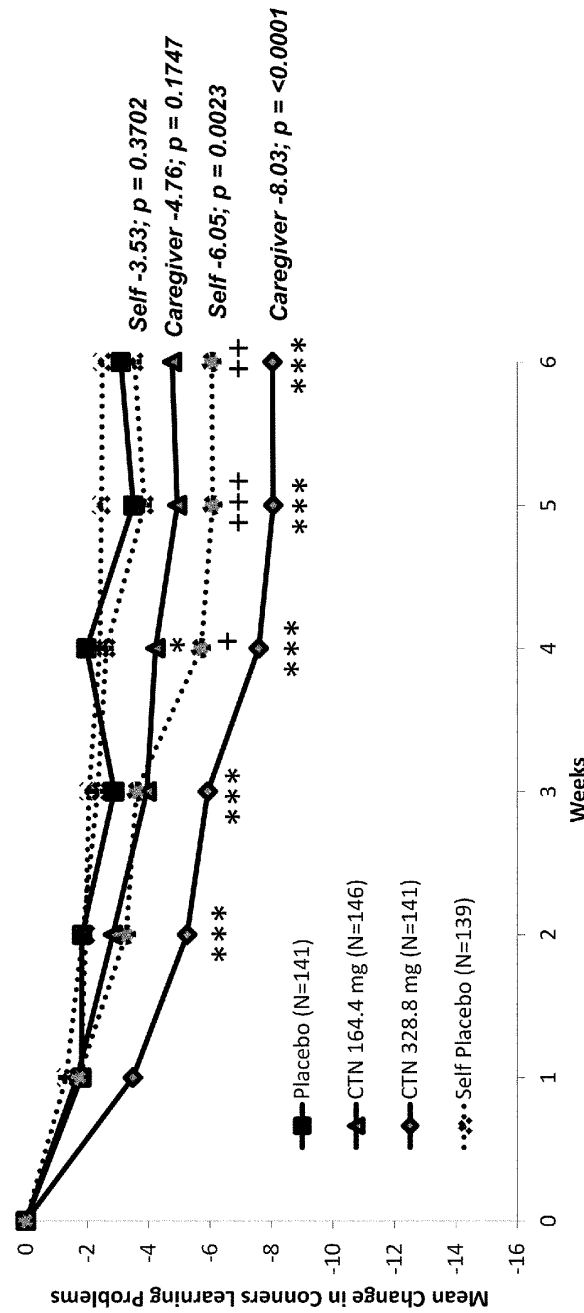


Baseline learning problems: Placebo = 65.96; CTN 164.4 mg QD XR = 66.29; CTN 328.8 mg QD XR = 66.04.
* nominal $p < 0.05$, ** nominal $p < 0.01$, *** nominal $p < 0.001$; CTN = centanafadine

FIGURE 28

[Fig. 29]

LSM Change from Baseline in Conners-3 Parent Short t-score Learning Problems Scale (MMRM) vs self report in adolescents



Caregiver report: Baseline learning problems: Placebo = 65.96; CTN 164.4 mg QD XR = 66.29; CTN 328.8 mg QD XR = 66.04. CTN = centanafadine. * nominal $p < 0.05$, ** nominal $p < 0.01$, *** nominal $p < 0.001$;
Self report Baseline: Placebo = 62.72; CTN 164.4 mg QD XR = 63.63; CTN 328.8 mg QD XR = 62.85; * nominal $p < 0.05$, ** nominal $p < 0.01$, *** nominal $p < 0.001$
-Subjects rated themselves as being less severe than their caregiver's rating at baseline

FIGURE 29

[Fig. 30]

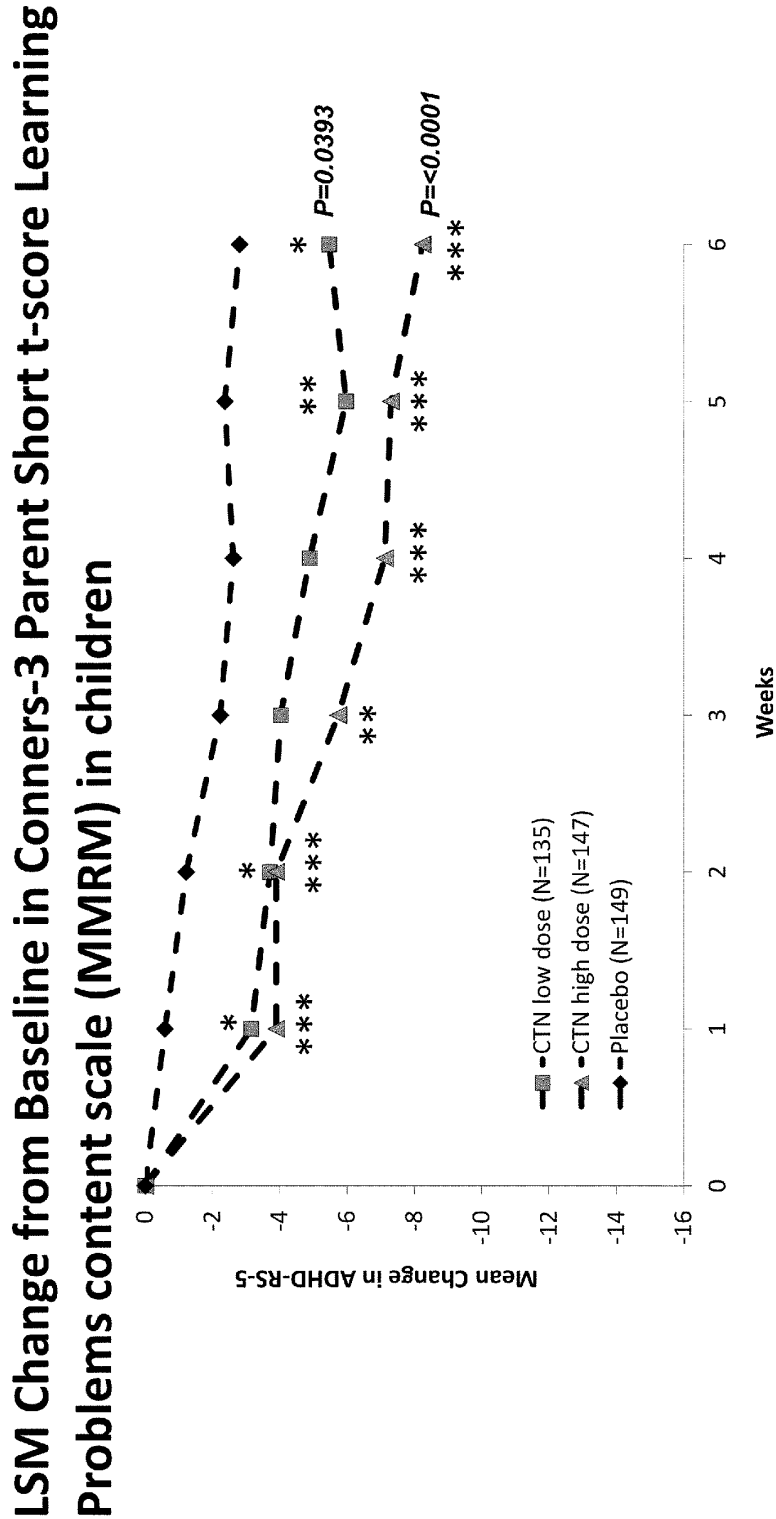
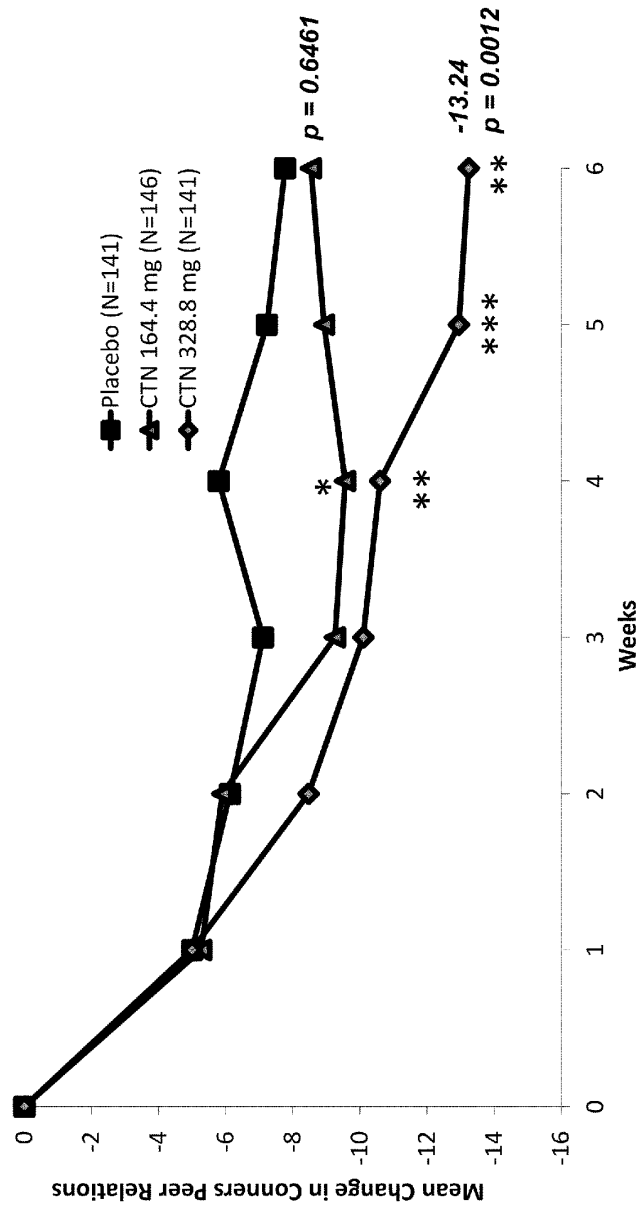


FIGURE 30

[Fig. 31]

LSM Change from Baseline in Conners-3 Parent Short t-score Peer Relations Content Scale (MMRM) in Adolescents



Baseline peer relations: Placebo = 67.49; CTN 164.4 mg QD XR = 68.92; CTN 328.8 mg QD XR = 67.50.

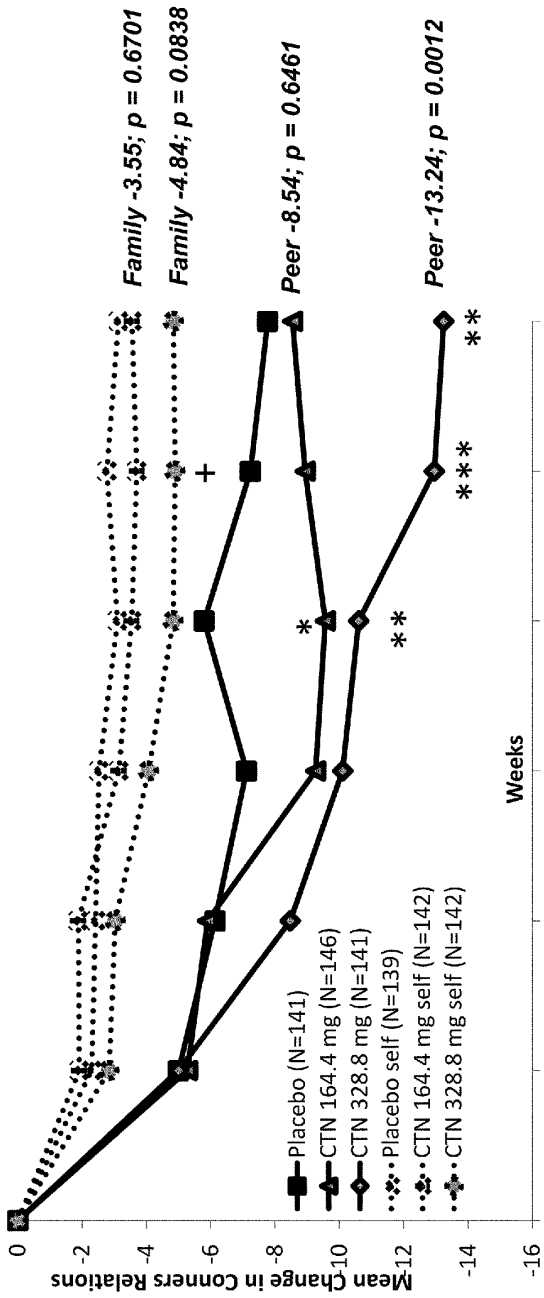
* nominal $p < 0.05$, ** nominal $p < 0.01$, *** nominal $p < 0.001$;

FIGURE 31

[Fig. 32]

* nominal $p < 0.05$, ** nominal $p < 0.01$, *** nominal $p < 0.001$;

LSM Change from Baseline in Conners-3 Parent Short t-score Peer Relations
Content Scale (MMRM) vs family relations self report (adolescent)



Caregiver baseline peer relations: Placebo = 67.49; CTN 164.4 mg QD XR = 68.92; CTN 328.8 mg QD XR = 67.50.

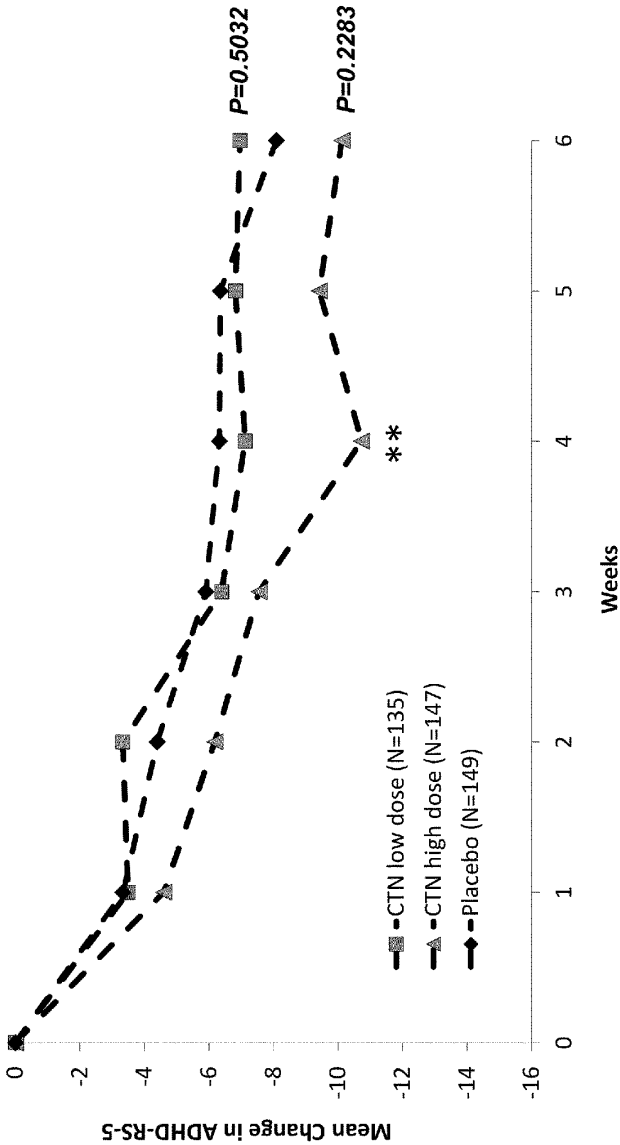
Self Baseline family relations: Placebo = 53.63; CTN 164.4 mg QD XR = 53.61; CTN 328.8 mg QD XR = 54.97.

-Subjects rated themselves as being less severe for family relations at baseline than their caregiver did for peer relations at baseline

FIGURE 32

[Fig. 33]

LSM Change from Baseline in Conners-3 Parent Short t-score Peer Relations content scale (MMRM) in children

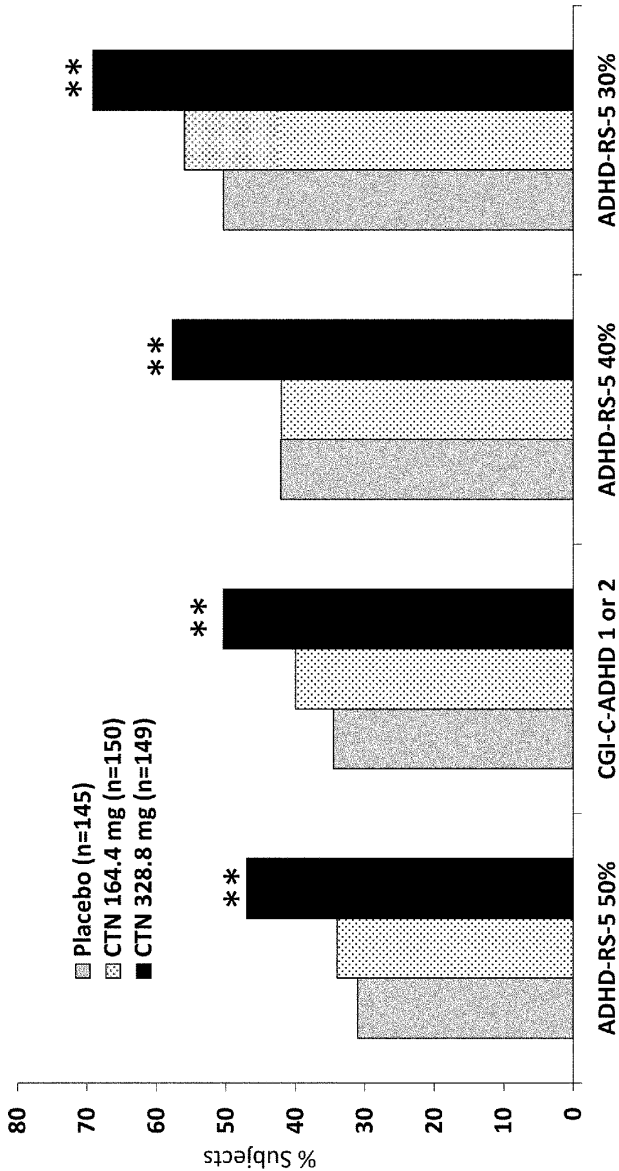


Baseline: Placebo = 72.15; CTN QD XR low = 70.70; CTN QD XR high = 68.39
* nominal p < 0.05, ** nominal p < 0.01, *** nominal p < 0.001; CTN = centanafadine

FIGURE 33

[Fig. 34]

Subjects achieving a 30%, 40% or 50% Response or CGI-C-ADHD of 1 or 2 at Week 6, LOCF Adolescents

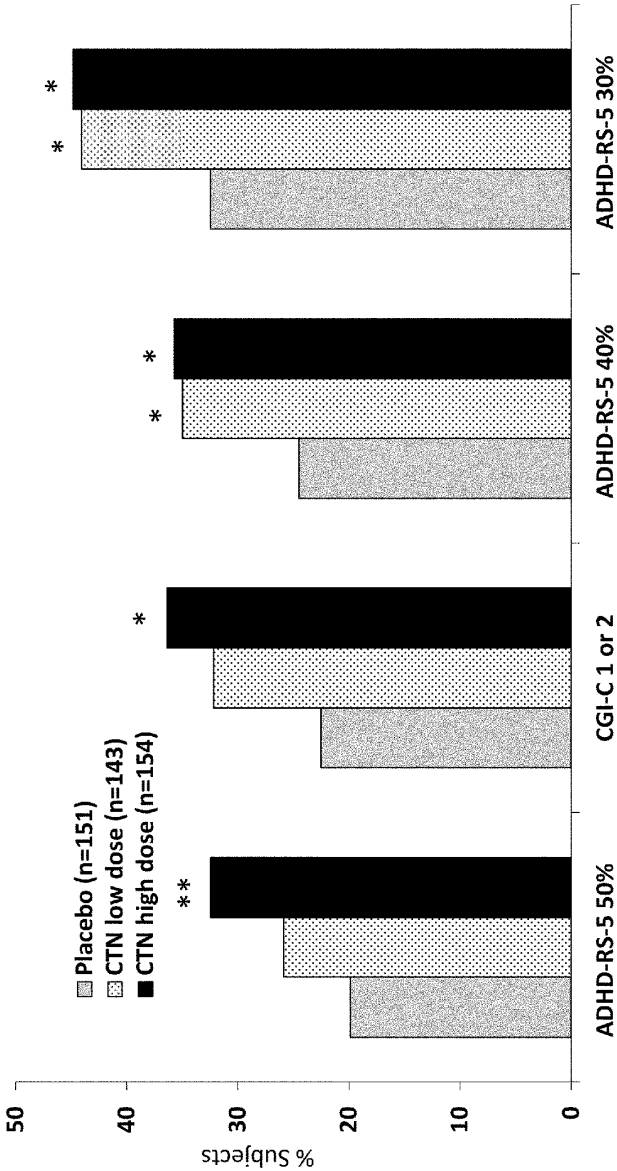


Cochran-Mantel-Haenszel. **nominal p < 0.01; CTN = centanafadine; LOCF = Last observation carried forward

FIGURE 34

[Fig. 35]

Subjects achieving a 30%, 40% or 50% Response or CGI-C-ADHD of 1 or 2 at Week 6, LOCF Children



Cochran-Mantel-Haenszel. * nominal $p < 0.05$, ** nominal $p < 0.01$; CTN = centanafadine

FIGURE 35

[Fig. 36]

LSM Change from Baseline in ADHD-RS-5 Total Raw Score (MMRM) In Adolescents by sex assigned at birth

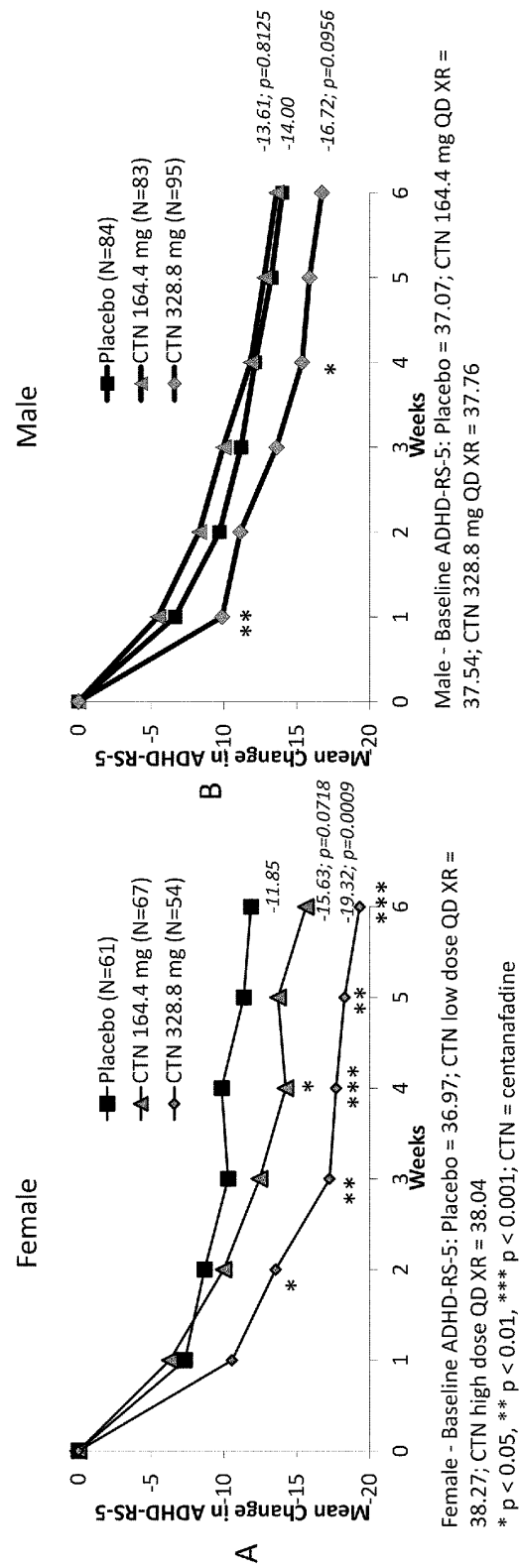
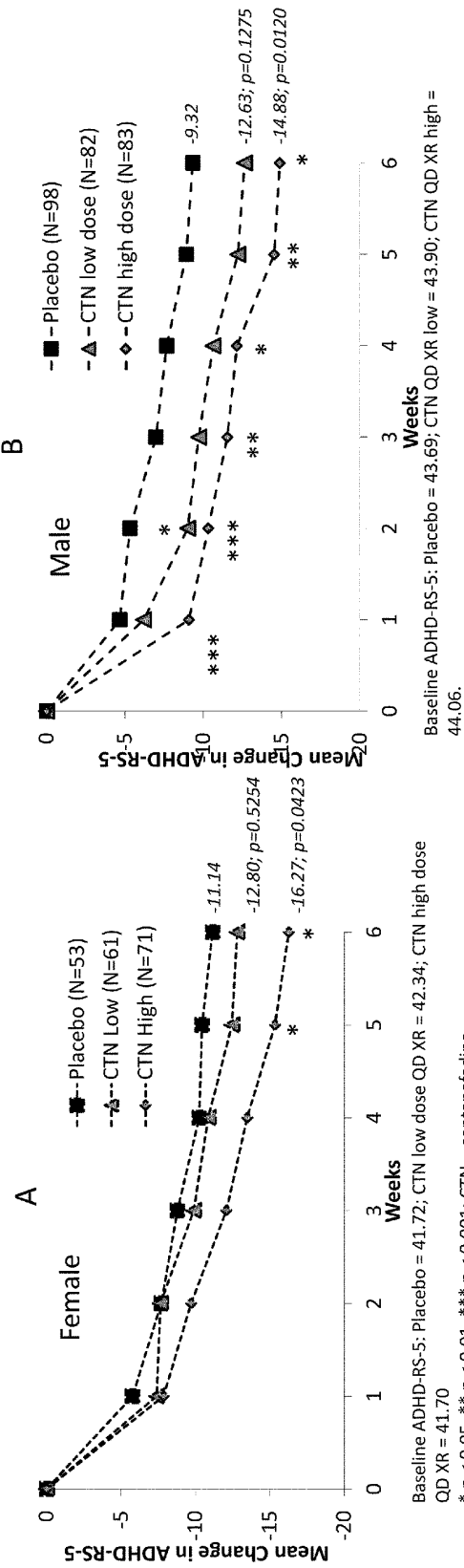


FIGURE 36A-B

[Fig. 37]

Primary Endpoint: LSM Change from Baseline in ADHD-RS-5 Total Raw Score (MMRM)
In Children by sex assigned at birth



• Males were more severe at baseline

FIGURE 37A-B

[Fig. 38]

LSM Change from Baseline in ADHD-RS-5 Total Raw Score (MMRM) in Adolescents by Race

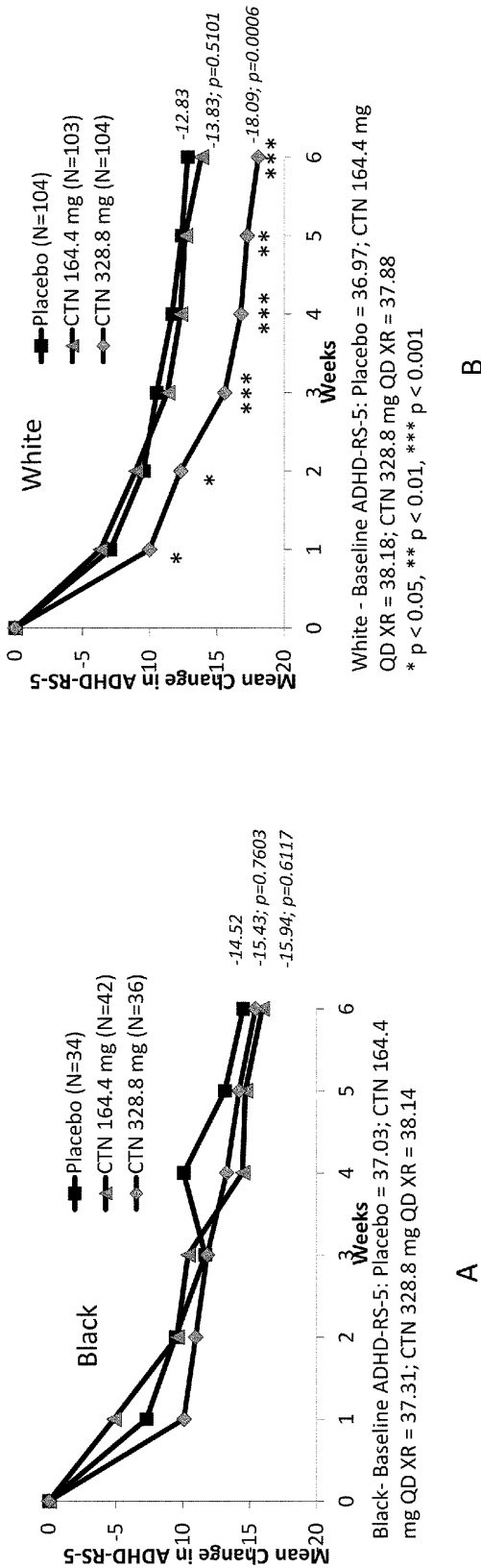
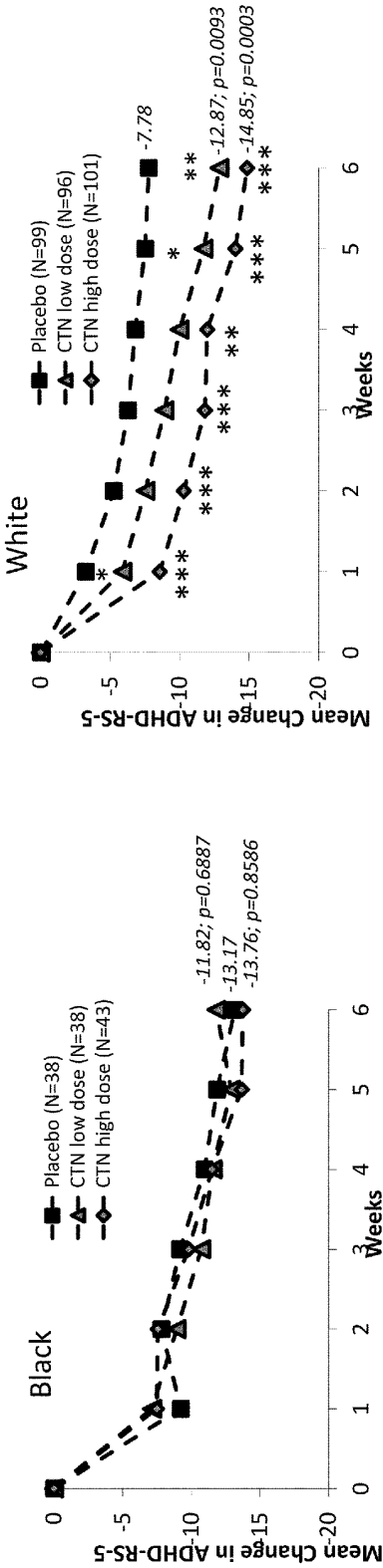


FIGURE 38A-B

[Fig. 39]

Primary Endpoint: LSM Change from Baseline in ADHD-RS-5 Total Raw Score (MMRM) in Children by Race

* p < 0.05, ** p < 0.01, *** p < 0.001; CTN = centanafadine



Black or African American: Baseline ADHD-RS-5: Placebo = 42.68; CTN QD XR low = 45.05; CTN QD XR high = 42.40.

White: Baseline ADHD-RS-5: Placebo = 42.64; CTN QD XR low = 42.22; CTN QD XR high = 42.74.

A B

FIGURE 39A-B

[Fig. 40]

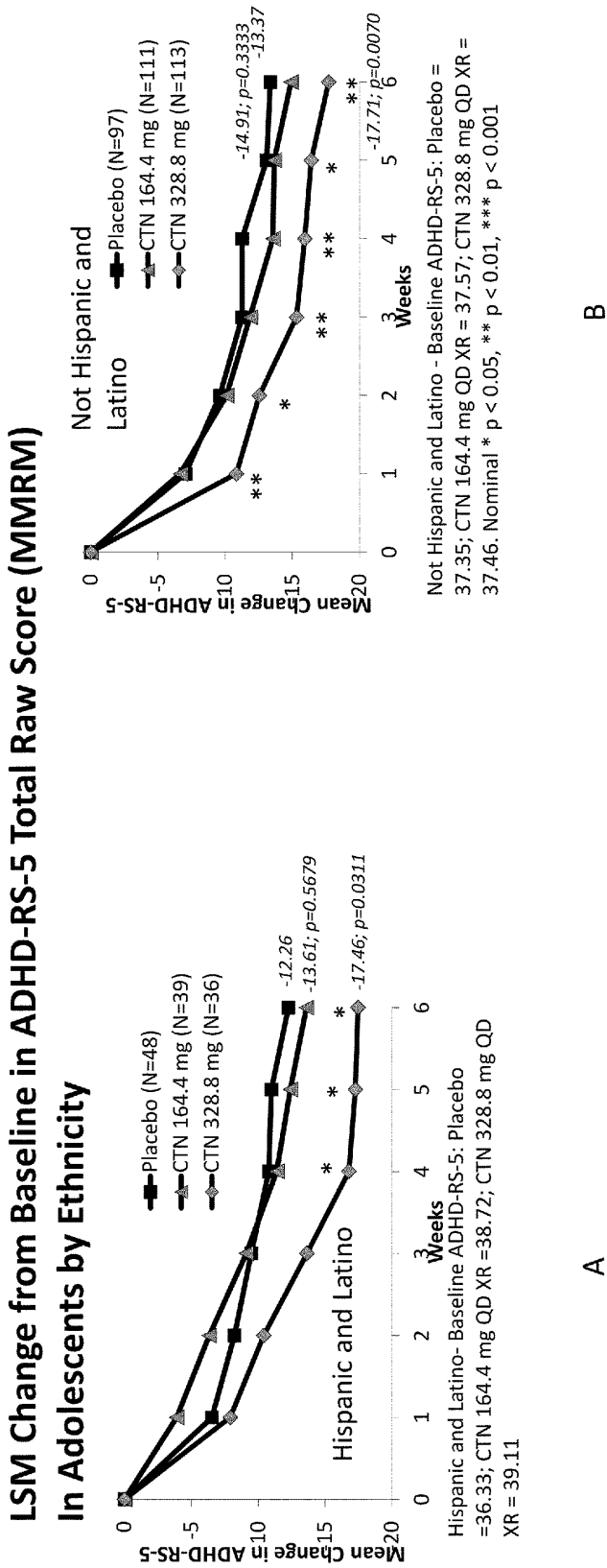


FIGURE 40A-B

[Fig. 41]

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$; CTN = centanafadine

**Primary Endpoint: LSM Change from Baseline in ADHD-RS-5 Total Raw Score (MMRM)
For Children by Ethnicity**

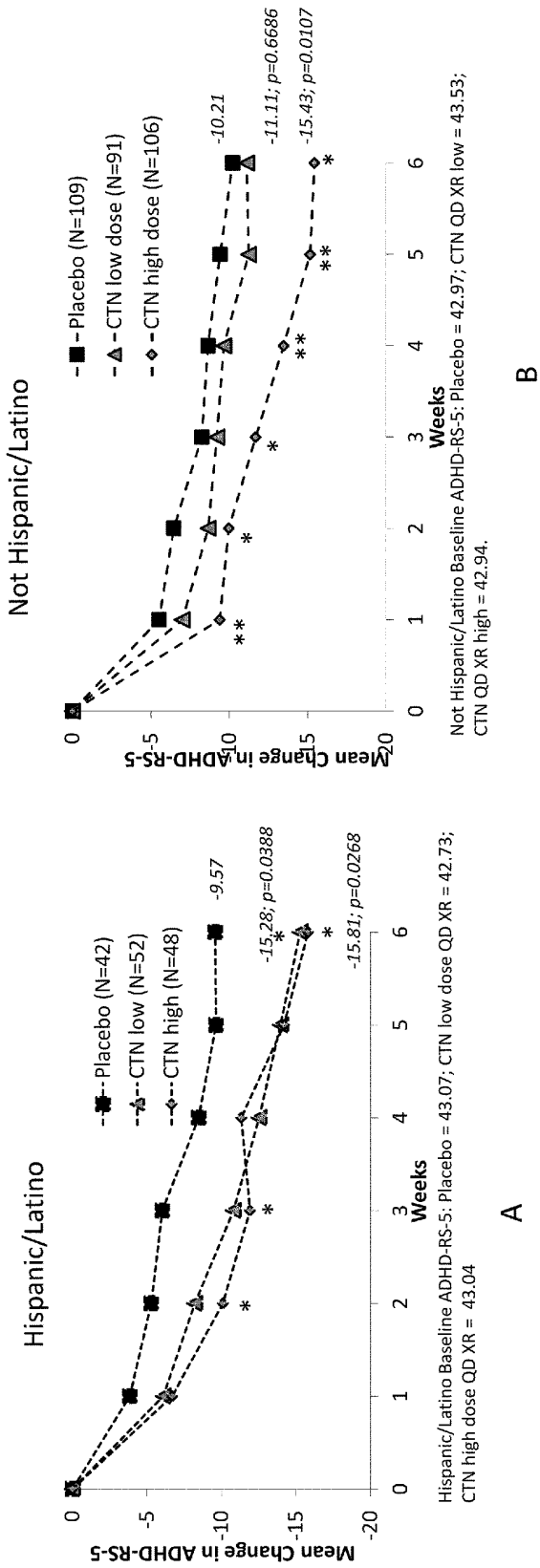


FIGURE 41A-B

[Fig. 42]

Quality of Life Assessment at Week 6 – Pediatric Quality of Life Family Impact Module 2.0

	Adolescents		Children	
	164.4 mg	328.8 mg	Low dose	High Dose
Mean change from baseline			Placebo	Placebo
Parent Health Related QoL	7.99 P=0.7468	12.66 P=0.0082	9.37 P=0.1070	9.11 P=0.1378
Family Functioning Summary Score	8.22 P=0.3848	14.29 P=0.0008	6.93 P=0.5790	11.61 P=0.0135
Total Score	6.87 P=0.5075	11.99 P=0.0006	7.09 P=0.1048	8.18 P=0.0309
				5.82
				5.60
				3.87

FIGURE 42

[Fig. 43]

ADHD-RS-5 Impairment Subscale Scores at Week 6

Mean change from baseline	Adolescents			Children		
	164.4 mg	328.8 mg	Placebo	Low dose CTN	High dose CTN	Placebo
Family relations	-0.81 P=0.6923	-0.90~ P=0.2033	-0.78	-0.69 P=0.4164	-0.72 P=0.3009	-0.60
Peer relations	-0.61 P=0.9126	-0.73 P=0.1814	-0.62	-0.64 P=0.7984	-0.77 P=0.1463	-0.61
Homework	-0.97 P=0.9715	-1.15 P=0.2088	-0.96	-0.98 P=0.0217	-1.12 P=0.0014	-0.63
Academics	-0.94 P=0.1929	-0.96 P=0.1522	-0.76	-0.84 P=0.4358	-1.12 P=0.0064	-0.73
Behaviour	-0.74 P=0.5523	-0.78 P=0.3807	-0.66	-0.84# P=0.2403	-0.95^ P=0.0439	-0.68
Self esteem	-0.67 P=0.4243	-0.75 P=0.8850	-0.74	-0.68 P=0.9024	-0.73 P=0.5282	-0.67

^nominal significance at weeks 1, 2, 4, 5, 6

FIGURE 43

[Fig. 44]

Incidence of Adverse Events - All Causalities - Adolescents

	CTN 164.4 mg n (%)	CTN 328.8 mg n (%)	Placebo n (%)	Total n (%)
Subjects Treated	153	151	147	451
Subjects with TEAEs	48 (31.4%)	76 (50.3%)	35 (23.8%)	159 (35.3%)
TEAEs	86	146	61	293
Subjects with Serious TEAEs	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Subjects with Severe TEAEs	2 (1.3%)	0 (0.0%)	1 (0.7%)	3 (0.7%)
Subjects Discontinued due to AE	5 (3.3%)	12 (7.9%)	0 (0.0%)	17 (3.8%)
Subject Deaths	0	0	0	0

Severe: LFT increase - low dose; aggression – low dose; somnolence – placebo
AEs leading to ET – low dose 1xelevated CPK, increased LFT and hepatitis; headache; rash; aggression; frequent bowel
movements and sedation
High: 3xrash; hypersensitivity; 3x decreased appetite; 3xnausea; HR inc on standing; inc BP; somnolence2; abd
discomfort; elevated CPK

CTN = centanafadine; TEAE= treatment emergent adverse event

FIGURE 44

[Fig. 45]

Incidence of Adverse Events - All Causalities - Children

	CTN low dose n (%)	CTN high dose n (%)	Placebo n (%)	Total n (%)
Subjects Treated	147	157	153	457
Subjects with TEAEs	52 (35.4%)	61 (38.9%)	39 (25.5%)	152 (33.3%)
TEAEs	93	110	69	272
Subjects with Serious TEAEs	3 (2.0%)	1 (0.6%)	0 (0.0%)	4 (0.9%)
Subjects with Severe TEAE	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.2%)
Subjects Discontinued due to AE	4 (2.7%)	10 (6.4%)	2 (1.3%)	16 (3.5%)
Subject Deaths	0	0	0	0

- 11y male randomized to high dose CTN experienced a moderate SAE of suicide attempt considered not related; drug was withdrawn.
- 10y female randomized to low dose CTN experienced a moderate SAE of suicide attempt considered not related; subject had completed dosing.
- 10y female randomized to low dose experienced a severe SAE of appendicitis considered not related.
- 10y male randomized to low dose experienced a mild SAE of panic attack considered not related; dose not changed

AEs leading to ET: placebo: FFEET LABILITY, DEPRESSION

Low dose: 3xrash; mood altered

High dose: 4xrash; neutropenia; diarrhea/headache/irritability; suicide attempt; COVID; dizziness/lethargy/nausea; blood pressure increased

CTN = centanafadine; TEAE= treatment emergent adverse event

FIGURE 45

[Fig. 46]

Most Common TEAEs >2% in CTN and greater than placebo

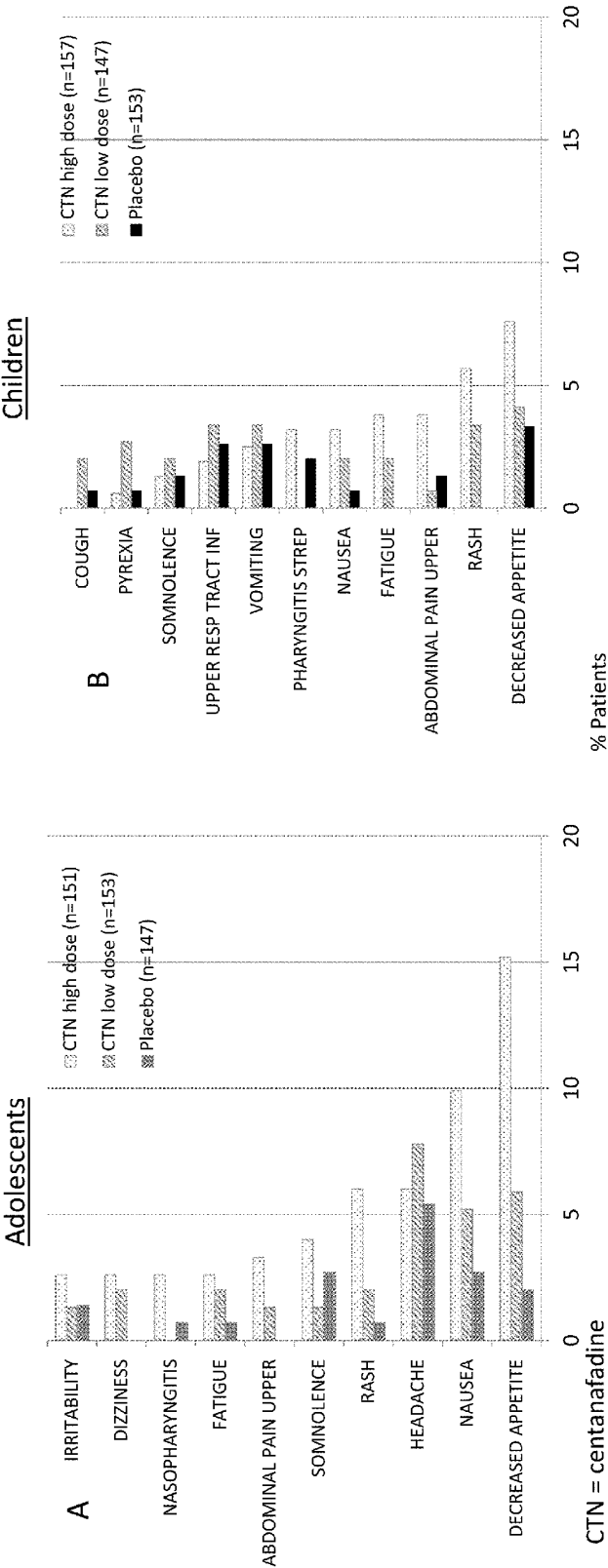


FIGURE 46A-B

[Fig. 47]

Most Common TEAEs >2% in CTN and greater than placebo Adolescents

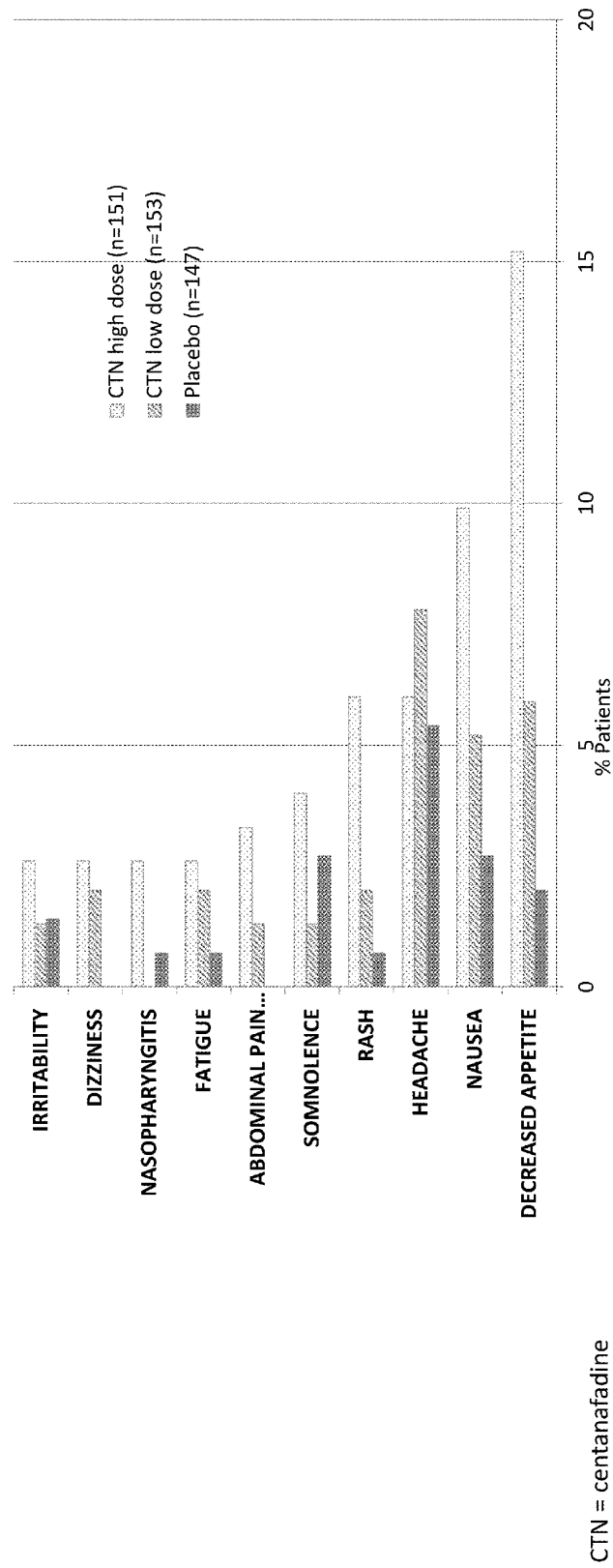


FIGURE 47

[Fig. 48]

Most Common TEAEs >2% in CTN and greater than placebo Children

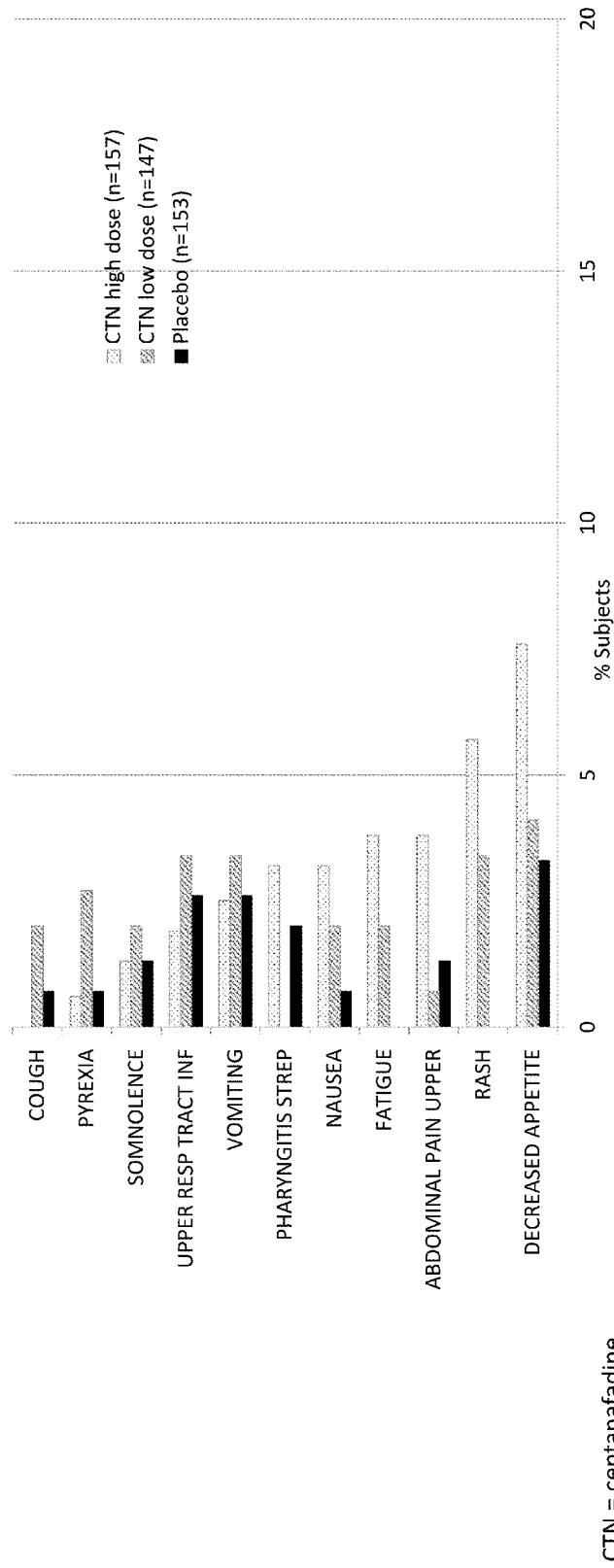


FIGURE 48

[Fig. 49]

Adverse Events Related to Suicidality

Item	Adolescents			Children	
	164.4 mg	328.8 mg	Placebo	Low	High
AE Suicide Behavior	0	0	1	1*	1*
AE Suicidal Ideation	1	1	1	0	0

Adolescents: Low dose ideation moderate; all others mild; all events considered non serious; high dose ideation potentially related

Children: both moderate; high dose ET, low dose already completed; both considered not related

*subjects were from the same site and events occurred in a similar timeframe; site denied subjects knowing each other

FIGURE 49

[Fig. 50]

Incidence of TEAEs - Abuse potential related					021 n (%)			BOLD = severe <i>Italics</i> = moderate	
					016 n (%)				
					164.4 mg N=153	328.8 N=151	Placebo N=147	Low N=147	High N=157
Subjects with any APR TEAE					8 (5.2)	12 (7.9)	5 (3.4)	5 (3.4)	3 (1.9)
Nervous system disorders					7 (4.6)	11 (7.3)	4 (2.7)	4 (2.7)	3 (1.9)
Dizziness					3 (2.0)	4 (2.6) <i>1xmod</i>	0 (0.0)	1 (0.7)	1 (0.6) <i>1xmod</i>
Hypersomnia					0 (0.0)	2 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)
Sedation					2 (1.3) <i>1xmod</i>	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
Somnolence					2 (1.3) <i>1xmod</i>	6 (4.0) <i>3xmod</i>	4 (2.7) <i>1xsev</i>	3 (2.0)	2 (1.3) <i>1xmod</i>
Psychiatric disorders					1 (0.7)	2 (1.3)	1 (0.7)	1 (0.7)	0 (0.0)
Aggression					1 (0.7) <i>1xsev</i>	0 (0.0)	1 (0.7) <i>1xmod</i>	0 (0.0)	0 (0.0)
Hallucination					0 (0.0)	1 (0.7)*	0 (0.0)	0 (0.0)	0 (0.0)
Mood Altered/Swings					0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)	0 (0.0)

*Mild (seeing things appear and then disappear)

FIGURE 50

[Fig. 51]

AE of Special Interest (Rash) Children and Adolescents						
Item	Adolescents n (%)			Children n (%)		
	164.4 mg	328.8 mg	Placebo	Low	High	Placebo
Any AEs	3 (2.0)	14 (9.3)	1 (0.7)	8 (5.4)	16 (10.2)	0 (0.0)
General Disord / Site admin cond						
Fatigue				0 (0.0)	1 (0.6)	0 (0.0)
Infections and infestations				0 (0.0)	1 (0.6)	0 (0.0)
Molluscum Contagiosum				0 (0.0)	1 (0.6)	0 (0.0)
Immune System Disorders	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	<u>1 (0.6) mod</u>	0 (0.0)
Hypersensitivity	0 (0.0)	<u>1 (0.7) mod</u>	0 (0.0)			
Skin and Subcutaneous Tissue Disor	3 (2.0)	13 (8.6)	1 (0.7)	8 (5.4)	14 (8.9)	0 (0.0)
Dermatitis	0 (0.0)	1 (0.7)	0 (0.0)			
Drug Eruption				<u>1 (0.7) mod</u>	0 (0.0)	0 (0.0)
Rash	3 (2.0)	<u>9 (6.0) 4xmod</u>	1 (0.7)	5 (3.4)	<u>9 (5.7) 1xmod</u>	0 (0.0)
Rash Macular				1 (0.7)	0 (0.0)	0 (0.0)
Rash Maculo-papular	0 (0.0)	3 (2.0)	0 (0.0)	<u>1 (0.7) mod</u>	3 (1.9)	0 (0.0)
Rash Morbilliform				0 (0.0)	1 (0.6)	0 (0.0)
Rash Papular				0 (0.0)	1 (0.6)	0 (0.0)

FIGURE 51