The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

GSK Medicine: Not applicable	

GSK Medicine: Not applicable

Study Number: 205703

Title: A study to evaluate potential biomarkers of muscular dystrophy

Rationale: This study was undertaken to explore whether tetranor prostaglandin D2 metabolite (PGDM) levels are increased in urine of males affected with muscular dystrophy (MD), specifically Duchenne muscular dystrophy (DMD), when compared to healthy, age-matched volunteers. It was expected that data from this study would be used to determine whether tetranor PGDM might be a useful marker of pharmacodynamic activity for experimental therapies that act on the PGD2 pathway in both preclinical and clinical studies in DMD.

Phase: N/A

Study Period: 14-Oct-2016 to 20-Apr-2018

Study Design: This was a non-interventional, cross-sectional study in male subjects with DMD and age-matched healthy male subjects. No treatments were administered. From each subject, two urine samples were collected at Baseline on two separate days (5 to 15 days apart). Subjects with DMD had an additional follow-up visit 12 months (±1 month) after Baseline, during which another urine sample was collected.

Centers: The study was conducted at two centers in the United States.

Indication: Muscular Dystrophies

Treatment: No treatments were administered.

Objectives:
Primary: To examine urine levels of creatinine and tetranor PGDM in healthy males and males with Muscular Dystrophy.
Secondary: To examine the relationship between tetranor PGDM (and other biomarkers, data permitting) and ambulatory status in DMD subjects.
Exploratory: To examine the relationship between tetranor PGDM and creatinine in urine.
To examine urine levels of additional prostaglandin metabolites in healthy males and males with Muscular Dystrophy.

Primary Outcome (Endpoints): Measurement of urine levels of creatinine and tetranor PGDM (corrected) at Baseline.

Secondary Outcome (Endpoints):
- Ambulatory status and urine biomarker levels at Baseline and approximately 12 months after collection of the first urine sample.
- Change from Baseline in urine biomarkers.
- Change from Baseline ambulatory status.

Exploratory Outcome (Endpoints):
- Urine levels of creatinine and tetranor PGDM (uncorrected).
- Measurement of urine levels of additional prostaglandin metabolites such as prostaglandin E2 metabolite (PGEM).

Statistical Methods:
Primary analyses: Levels of PGDM in subjects with DMD and age-matched male healthy volunteers (HV) were compared. A mixed effect, repeated measures model was used fitting fixed effect for population and age-group and population-by-age-group interaction and random effect for subject. Least squares means and 95% confidence intervals (CIs) were presented for each population. Differences in least squares means between subjects with DMD and age matched male HV were determined along with a 95% CI.

Secondary analyses: Relationship between tetranor PGDM level (and other biomarkers including prostaglandin metabolites) and ambulatory status in DMD subjects was explored: PGDM level and ambulatory status at Baseline and 12 months, Baseline PGDM level and change in ambulatory status, change in PGDM level and change in ambulatory status.

Other analyses: The relationship between uncorrected PGDM and PGEM with creatinine and osmolality were explored. Differences between genotypes were explored. Genotypes were grouped as:
- Deletion–any genotype with the word "deletion" in it
- Duplication–any genotype with the word "duplication" in it.
- Other–all other genotypes

The analysis populations included:
- All Subjects Population which comprised of all enrolled subjects.
- Biomarker Population which comprised of subjects in the 'All Subjects' population with non-missing results for tetranor PGDM and creatinine from at least one assessment.

Study Population: Male subjects aged 5 to 16 years (inclusive), with a diagnosis of DMD or healthy based on medical history were included. Healthy subjects had no known myopathy/muscular dystrophy or muscle contractures (cerebral palsy). Subjects were allowed to participate in this study only once.

	HV	DMD subjects
Number of Subjects (All Subjects Population)	37	42
Planned, N	40	40
Entered, N	37	42
Completed, n (%)	35 (95)	39 (93)
Total Number Subjects Withdrawn, N (%)	2 (5)	3 (7)
Withdrew consent n (%)	1 (3)	3 (7)
Lost to follow-up n (%)	1 (3)	0 (0)
Demographics	HV	DMD subjects
N (All Subjects Population)	37	42
Males	37	42
Mean Age, years (SD)	10.5 (3.23)	10.4 (3.15)
Race, n (%)		
African American/African Heritage	7 (19)	3 (7)
Asian-East Asian Heritage	0 (0)	1 (2)
Native Hawaiian or other Pacific Islander	1 (3)	1 (2)
White- White/Caucasian/European Heritage	28 (76)	37 (88)
Mixed Race	1 (3)	0 (0)

SD: standard deviation

Primary Outcome Results:

Urine levels of creatinine and tetranor PGDM (corrected) at Baseline (Biomarker Population)

Parameter	HV				DMD subjects			
	5-8 years Mean (SD)	9-11 years Mean (SD)	12-16 years Mean (SD)	Total Mean (SD)	5-8 years Mean (SD)	9-11 years Mean (SD)	12-16 years Mean (SD)	Total Mean (SD)
	n=10	n=8	n=15	n=33	n=10	n=12	n=16	n=38
Creatinine (mg/mL)	1.30950 (0.296961)	1.14894 (0.312835)	1.68357 (0.566765)	1.44061 (0.490973)	0.79680 (0.308449)	0.81796 (0.259762)	0.68221 (0.341084)	0.75523 (0.307272)
Corrected PGDM for Creatinine (ng/mg Crn)	1.02675 (0.400487)	1.40920 (0.621025)	0.99310 (0.427659)	1.10417 (0.490313)	2.21364 (0.818161)	2.58654 (1.628458)	3.28657 (1.933674)	2.78316 (1.636110)
Corrected PGDM for Osmolality (ng/mg Osm) [a]	0.00133 (0.000572)	0.00194 (0.001204)	0.00182 (0.000925)	0.00170 (0.000920)	0.00179 (0.000683)	0.00239 (0.001709)	0.00244 (0.001307)	0.00225 (0.001324)

Summary of Repeated Measures Analysis of Urine Biomarkers Comparing DMD Subjects with HV (Biomarker Population)				
Age Group		DMD N=39	HV N=35	Difference (DMD–HV)
Parameter: PGDM Corrected for Creatinine (ng/mg Crn)				

5-8 years	n	10	10	
	Adj. Mean (SE)	2.2103 (0.3961)	1.0388 (0.1643)	1.1716 (0.4288)
	95% CI	(1.4197, 3.0009)	(0.7109, 1.3666)	(0.3157, 2.0274)
9-11 years	n	12	8	
	Adj. Mean (SE)	2.5851 (0.3601)	1.4092 (0.1815)	1.1759 (0.4032)
	95% CI	(1.8664, 3.3039)	(1.0470, 1.7714)	(0.3710, 1.9808)
12-16 years	n	16	15	
	Adj. Mean (SE)	3.2866 (0.3057)	0.9991 (0.1336)	2.2875 (0.3336)
	95% CI	(2.6764, 3.8968)	(0.7324, 1.2657)	(1.6216, 2.9534)
Total	n	38	33	
	Adj. Mean (SE)	2.6940 (0.2055)	1.1490 (0.0930)	1.5450 (0.2255)
	95% CI	(2.2839, 3.1041)	(0.9635, 1.3345)	(1.0948, 1.9951)
Parameter: PGDM Corrected for Osmolality (ng/mg Osm) [a]				
5-8 years	n	10	10	
	Adj. Mean (SE)	0.0018 (0.0004)	0.0013 (0.0003)	0.0004 (0.0005)
	95% CI	(0.0010, 0.0025)	(0.0006, 0.0020)	(-0.0006, 0.0014)
9-11 years	n	12	8	
	Adj. Mean (SE)	0.0024 (0.0003)	0.0019 (0.0004)	0.0004 (0.0005)
	95% CI	(0.0017, 0.0031)	(0.0012, 0.0027)	(-0.0006, 0.0015)
12-16 years	n	16	15	
	Adj. Mean (SE)	0.0024 (0.0003)	0.0018 (0.0003)	0.0006 (0.0004)
	95% CI	(0.0019, 0.0030)	(0.0013, 0.0024)	(-0.0002, 0.0014)
Total	n	38	33	
	Adj. Mean (SE)	0.0022 (0.0002)	0.0017 (0.0002)	0.0005 (0.0003)
	95% CI	(0.0018, 0.0026)	(0.0013, 0.0021)	(-0.0001, 0.0010)
Parameter: Creatinine (mg/mL)				
5-8 years	n	10	10	
	Adj. Mean (SE)	0.7976 (0.1055)	1.3095 (0.1282)	-0.5119 (0.1660)
	95% CI	(0.5871, 1.0081)	(1.0536, 1.5654)	(-0.8432, -0.1806)
9-11 years	n	12	8	
	Adj. Mean (SE)	0.8174 (0.0962)	1.1489 (0.1434)	-0.3315 (0.1726)
	95% CI	(0.6255, 1.0093)	(0.8629, 1.4350)	(-0.6760, 0.0129)
12-16 years	n	16	15	
	Adj. Mean (SE)	0.6822 (0.0828)	1.6775 (0.1058)	-0.9953 (0.1343)
	95% CI	(0.5170, 0.8474)	(1.4665, 1.8886)	(-1.2634, -0.7273)
Total	n	38	33	
	Adj. Mean (SE)	0.7657 (0.0550)	1.3787 (0.0732)	-0.6129 (0.0915)
	95% CI	(0.6560, 0.8755)	(1.2327, 1.5247)	(-0.7956, -0.4303)

a: exploratory results presented for practical purpose; mg/mL: milligrams per milliliter; ng/mg: nanograms per milligram; Crn: creatinine; Osm: osmolality; SE: standard error; adj.: adjusted

Secondary Outcome Results:

Summary of urine biomarkers by ambulatory status in DMD subjects (Biomarker Population)

Corrected PGDM for Creatinine (ng/mg Crn), N=39

Ambulatory Status	Relative time	n	Mean	SD
Stage 2 Early Ambulatory	Baseline*	13	2.11631	0.745924
	Follow-up	8	1.64835	0.383459
Stage 3 Late Ambulatory	Baseline*	12	1.95132	0.764076
	Follow-up	14	1.95103	0.391006
Stage 4 Early Non-Ambulatory	Baseline*	7	4.12892	1.823106
	Follow-up	8	2.54343	0.886899
Stage 5 Late Non-Ambulatory	Baseline*	6	4.32162	2.237831
	Follow-up	8	5.61695	2.915860

Corrected PGDM for Osmolality (ng/mg Osm), N=39

Ambulatory Status	Relative time	n	Mean	SD
Stage 2 Early Ambulatory	Baseline*	13	0.00178	0.000678
	Follow-up	8	0.00147	0.000289
Stage 3 Late Ambulatory	Baseline*	12	0.00186	0.000681
	Follow-up	13	0.00192	0.000705
Stage 4 Early Non-Ambulatory	Baseline*	7	0.00374	0.002231
	Follow-up	8	0.00197	0.000759
Stage 5 Late Non-Ambulatory	Baseline*	6	0.00235	0.000907
	Follow-up	8	0.00254	0.001555

Corrected Prostaglandin E2 metabolite (PGEM) for Creatinine (ng/mg Crn), N=39				
Stage 2 Early Ambulatory	Baseline*	13	19.39571	12.694177
	Follow-up	8	10.69897	4.831841
Stage 3 Late Ambulatory	Baseline*	12	13.40343	5.227326
	Follow-up	14	18.06272	11.109556
Stage 4 Early Non-Ambulatory	Baseline*	7	36.99188	19.677303
	Follow-up	8	31.69086	29.160883
Stage 5 Late Non-Ambulatory	Baseline*	6	41.85093	38.047070
	Follow-up	8	49.79457	19.765477
Corrected PGEM for Osmolality (ng/mg Osm), N=39				
Stage 2 Early Ambulatory	Baseline*	13	0.01456	0.005677
	Follow-up	8	0.00973	0.004723
Stage 3 Late Ambulatory	Baseline*	12	0.01273	0.005086
	Follow-up	13	0.01740	0.008665
Stage 4 Early Non-Ambulatory	Baseline*	7	0.03556	0.024188
	Follow-up	8	0.02244	0.015488
Stage 5 Late Non-Ambulatory	Baseline*	6	0.01943	0.006472
	Follow-up	8	0.02141	0.006761
Creatinine (mg/mL), N=39				
Stage 2 Early Ambulatory	Baseline*	13	0.73085	0.250404
	Follow-up	8	0.94700	0.158333
Stage 3 Late Ambulatory	Baseline*	12	0.90404	0.309795
	Follow-up	14	0.80421	0.255553
Stage 4 Early Non-Ambulatory	Baseline*	7	0.79843	0.311191
	Follow-up	8	0.70700	0.229842
Stage 5 Late Non-Ambulatory	Baseline*	6	0.46005	0.242861
	Follow-up	8	0.39563	0.153542
Tetranor-Prostaglandin D Metabolite (ng/mL), N=39				
Stage 2 Early Ambulatory	Baseline*	13	1.45270	0.447725
	Follow-up	8	1.53878	0.349286
Stage 3 Late Ambulatory	Baseline*	12	1.60118	0.477229
	Follow-up	14	1.55216	0.571087
Stage 4 Early Non-Ambulatory	Baseline*	7	3.39917	2.489984
	Follow-up	8	1.72103	0.639091
Stage 5 Late Non-Ambulatory	Baseline*	6	1.65163	0.925879
	Follow-up	8	2.22096	1.679316
Tetranor-Prostaglandin E Metabolite (ng/mL), N=39				
Stage 2 Early Ambulatory	Baseline*	13	12.05931	5.044242
	Follow-up	8	10.15188	4.749255
Stage 3 Late Ambulatory	Baseline*	12	11.26542	5.410487
	Follow-up	14	13.64936	6.662819
Stage 4 Early Non-Ambulatory	Baseline*	7	33.71729	24.916968
	Follow-up	8	20.07400	13.707321
Stage 5 Late Non-Ambulatory	Baseline*	6	13.09750	5.545621
	Follow-up	8	18.12938	7.729121
Urine Osmolality (mmol/kg), N=39				
Stage 2 Early Ambulatory	Baseline*	14	860.93	187.095
	Follow-up	8	1049.00	116.473
Stage 3 Late Ambulatory	Baseline*	12	897.50	127.798
	Follow-up	13	881.00	165.619
Stage 4 Early Non-Ambulatory	Baseline*	7	896.07	203.752
	Follow-up	8	919.63	293.811
Stage 5 Late Non-Ambulatory	Baseline*	6	679.67	143.625
	Follow-up	8	846.13	169.873

*: Baseline is the mean of Day 1 and Week 2; ng/mL: nanograms per milliliter; mmol/kg: millimoles per kilogram

Repeated Measures Analysis of Corrected Urine Biomarkers over 12 months in DMD Subjects (Biomarker Population)

Age group		12 months	Baseline	Difference (12 months-Baseline)
Parameter: Corrected PGDM for Creatinine (ng/mg Crn)				
5-8 years	n	11	10	
	Adj. Mean (SE)	1.9237 (0.5436)	2.2046 (0.4926)	-0.2809 (0.4917)

	95% CI	(0.8385, 3.0088)	(1.2214, 3.1878)	(-1.2623, 0.7005)
9-11 years	n	11	12	
	Adj. Mean (SE)	2.2105 (0.5360)	2.5684 (0.4555)	-0.3579 (0.4728)
	95% CI	(1.1406, 3.2803)	(1.6591, 3.4776)	(-1.3017, 0.5859)
12-16 years	n	16	16	
	Adj. Mean (SE)	3.8711 (0.4508)	3.2866 (0.3906)	0.5845 (0.3898)
	95% CI	(2.9713, 4.7708)	(2.5070, 4.0662)	(-0.1935, 1.3625)
Total	n	38	38	
	Adj. Mean (SE)	2.6684 (0.2955)	2.6865 (0.2588)	-0.0181 (0.2619)
	95% CI	2.0785, 3.2583	(2.1700, 3.2030)	(-0.5408, 0.5046)
Parameter: Corrected PGDM for Osmolality (ng/mg Osm)				
5-8 years	n	10	10	
	Adj. Mean (SE)	0.0018 (0.0004)	0.0017 (0.0004)	0.0001 (0.0004)
	95% CI	(0.0010, 0.0026)	(0.0010, 0.0024)	(-0.0006, 0.0008)
9-11 years	n	11	12	
	Adj. Mean (SE)	0.0019 (0.0004)	0.0024 (0.0003)	-0.0005 (0.0003)
	95% CI	(0.0011, 0.0027)	(0.0017, 0.0030)	(-0.0012, 0.0002)
12-16 years	n	16	16	
	Adj. Mean (SE)	0.0022 (0.0003)	0.0024 (0.0003)	-0.0003 (0.0003)
	95% CI	(0.0015, 0.0028)	(0.0019, 0.0030)	(-0.0008, 0.0003)
Total	n	37	38	
	Adj. Mean (SE)	0.0020 (0.0002)	0.0022 (0.0002)	-0.0002 (0.0002)
	95% CI	(0.0015, 0.0024)	(0.0018, 0.0026)	(-0.0006, 0.0002)
Corrected PGEM for Creatinine (ng/mg Crn)				
5-8 years	n	11	10	
	Adj. Mean (SE)	14.8174 (6.6343)	22.0283 (5.9681)	-7.2109 (6.1607)
	95% CI	(1.5716, 28.0633)	(10.1126, 33.9440)	(-19.5110, 5.0893)
9-11 years	n	11	12	
	Adj. Mean (SE)	18.0733 (6.5498)	22.7192 (5.5103)	-4.6459 (5.9272)
	95% CI	(4.9962, 31.1505)	(11.7176, 33.7209)	(-16.4800, 7.1882)
12-16 years	n	16	16	
	Adj. Mean (SE)	39.1064 (5.5009)	26.4858 (4.7586)	12.6206 (4.9244)
	95% CI	(28.1236, 50.0893)	(16.9850, 35.9867)	(2.7887, 22.4525)
Total	n	38	38	
	Adj. Mean (SE)	23.9991 (3.6082)	23.7445 (3.1380)	0.2546 (3.2886)
	95% CI	(16.7950, 31.2031)	(17.4792, 30.0098)	(-6.3114, 6.8206)
Parameter: Corrected PGEM for Osmolality (ng/mg Osm)				
5-8 years	n	10	10	
	Adj. Mean (SE)	0.0141 (0.0041)	0.0158 (0.0035)	-0.0017 (0.0040)
	95% CI	(0.0059, 0.0222)	(0.0089, 0.0228)	(-0.0097, 0.0062)
9-11 years	n	11	12	
	Adj. Mean (SE)	0.0148 (0.0039)	0.0207 (0.0032)	-0.0059 (0.0037)
	95% CI	(0.0071, 0.0226)	(0.0143, 0.0271)	(-0.0133, 0.0014)
12-16 years	n	16	16	
	Adj. Mean (SE)	0.0216 (0.0033)	0.0177 (0.0028)	0.0040 (0.0031)
	95% CI	(0.0151, 0.0282)	(0.0121, 0.0232)	(-0.0021, 0.0101)
Total	n	37	38	
	Adj. Mean (SE)	0.0169 (0.0022)	0.0181 (0.0018)	-0.0012 (0.0021)
	95% CI	(0.0125, 0.0212)	(0.0144, 0.0217)	(-0.0054, 0.0029)
Parameter: Tetranor-Prostaglandin D Metabolite (ng/mL)				
5-8 years	n	11	10	
	Adj. Mean (SE)	1.5625 (0.3879)	1.5758 (0.3480)	-0.0133 (0.3639)
	95% CI	(0.7882, 2.3368)	(0.8813, 2.2703)	(-0.7396, 0.7130)
9-11 years	n	11	12	
	Adj. Mean (SE)	1.6185 (0.3832)	2.1081 (0.3211)	-0.4896 (0.3502)
	95% CI	(0.8537, 2.3833)	(1.4672, 2.7489)	(-1.1885, 0.2093)
12-16 years	n	16	16	
	Adj. Mean (SE)	1.9162 (0.3216)	1.9217 (0.2750)	-0.0055 (0.2889)
	95% CI	(1.2742, 2.5582)	(1.3727, 2.4707)	(-0.5820, 0.5711)
Total	n	38	38	
	Adj. Mean (SE)	1.6991 (0.2110)	1.8685 (0.1825)	-0.1694 (0.1939)

	95% CI	(1.2779, 2.1203)	(1.5042, 2.2328)	(-0.5565, 0.2176)
Parameter: Tetranor-Prostaglandin E Metabolite (ng/mL)				
5-8 years	n	11	10	
	Adj. Mean (SE)	11.7880 (3.8530)	14.3276 (3.4154)	-2.5396 (3.7523)
	95% CI	(4.0951, 19.4809)	(7.5085, 21.1467)	(-10.0313, 4.9521)
9-11 years	n	11	12	
	Adj. Mean (SE)	13.5880 (3.8133)	19.3886 (3.1442)	-5.8006 (3.6134)
	95% CI	(5.9746, 21.2014)	(13.1109, 25.6663)	(-13.0150, 1.4138)
12-16 years	n	16	16	
	Adj. Mean (SE)	18.2889 (3.1948)	13.7807 (2.7144)	4.5082 (3.0047)
	95% CI	(11.9104, 24.6675)	(8.3612, 19.2002)	(-1.4908, 10.5072)
Total	n	38	38	
	Adj. Mean (SE)	14.5550 (2.0974)	15.8323 (1.7926)	-1.2773 (2.0046)
	95% CI	(10.3673, 18.7427)	(12.2534, 19.4113)	(-5.2796, 2.7249)

Change from Baseline in corrected urine biomarkers at 12 months (Biomarker Population)

	DMD Subjects			
Parameter	5-8 years Mean (SD)	9-11 years Mean (SD)	12-16 years Mean (SD)	Total Mean (SD)
	n=10	n=11	n=16	n=37
Corrected PGDM for Creatinine (ng/mg Crn),	-0.29166 (0.835238)	-0.30417 (0.807632)	0.58451 (2.580027)	0.08351 (1.823659)
	n=9	n=11	n=16	n=36
Corrected PGDM for Osmolality (ng/mg Osm)	0.00004 (0.000867)	-0.00049 (0.001286)	-0.00026 (0.001333)	-0.00025 (0.001202)
	n=10	n=11	n=16	n=37
Corrected PGEM for Creatinine (ng/mg Crn)	-7.37403 (9.598547)	-5.83844 (19.388845)	12.79531 (30.463911)	1.80437 (24.679607)
	n=9	n=11	n=16	n=36
Corrected PGEM for Osmolality (ng/mg Osm)	-0.00227 (0.005783)	-0.00754 (0.022368)	0.00380 (0.013122)	-0.00118 (0.015772)

Change from Baseline in ambulatory status[b] in DMD subjects (All Subjects Population)

Ambulatory Status	5-8 years (N=12)	9-11 years (N=14)	12-16 years (N=16)	Total (N=42)
No Change	7 (64)	7 (64)	12 (75)	26 (68)
Any Change	4 (36)	4 (36)	4 (25)	12 (32)
Stage 2 Early Ambulatory-Stage 3 Late Ambulatory	4 (36)	2 (18)	0	6 (16)
Stage 3 Late Ambulatory-Stage 4 Early Non-Ambulatory	0	1 (9)	3 (19)	4 (11)
Stage 4 Early Non-Ambulatory-Stage 5 Late Non-Ambulatory	0	1 (9)	1 (6)	2 (5)

b: One subject in the 5 to 8 years age group and 3 subjects in the 9 to 11 years age group had missing ambulatory status at Follow-up.

Exploratory Outcome:

Summary of uncorrected urine biomarkers (Biomarker Population)

Parameter	5-8 years Mean (SD)		9-11 years Mean (SD)		12-16 years Mean (SD)		Total Mean (SD)	
	HV	DMD	HV	DMD	HV	DMD	HV	DMD
Tetranor PGDM (ng/mL)	n=10	n=10	n=8	n=12	n=15	n=16	n=33	N=38
Baseline *	1.23517 (0.541676)	1.56338 (0.393150)	1.53640 (0.632481)	2.11852 (1.740298)	1.53172 (0.564125)	1.92170 (1.408369)	1.44299 (0.573260)	1.88956 (1.337285)
	-	n=11	-	n=11	-	n=16	-	n=38
Follow-up	-	1.56251 (0.496449)	-	1.61173 (0.657193)	-	1.91623 (1.226293)	-	1.72569 (0.905796)
Tetranor PGEM (ng/mL)	n=10	n=10	n=8	n=12	n=15	n=16	n=33	n=38
Baseline *	14.27920 (6.124068)	13.96500 (5.541187)	10.93456 (4.712986)	20.24025 (21.292291)	18.08670 (14.122792)	14.00181 (10.458179)	15.19906 (10.554021)	15.96216 (13.973838)

	-	n=11	-	n=11	-	n=16	-	n=38
Follow-up	-	11.78800 (6.981827)	-	14.14927 (7.742630)	-	18.28894 (10.278868)	-	15.208761 (8.951271)
Creatinine (mg/mL)	n=10	n=10	n=8	n=12	n=15	n=16	n=33	n=38
Baseline *	1.30950 (0.296961)	0.79680 (0.308449)	1.14894 (0.312835)	0.81796 (0.259762)	1.68357 (0.566765)	0.68221 (0.341084)	1.44061 (0.490973)	0.75523 (0.307272)
	-	n=11	-	n=11	-	n=16	-	n=38
Follow-up	-	0.82355 (0.251238)	-	0.81855 (0.252215)	-	0.59956 (0.281632)	-	0.72779 (0.280522)
Urine Osmolality (mmol/kg)	n=11	n=11	n=9	n=12	n=15	n=16	n=35	n=39
Baseline *	951.64 (180.507)	925.59 (197.258)	876.89 (159.986)	889.58 (155.240)	907.97 (220.421)	769.81 (156.183)	913.70 (190.920)	850.60 (178.046)
	-	n=10	-	n=11	-	n=16	-	n=37
Follow-up	-	974.10 (180.296)	-	937.64 (259.463)	-	869.75 (160.850)	-	918.14 (199.083)

Summary of Urine biomarkers by genotype in DMD subjects (Biomarker Population):

Parameter: Creatinine (mg/mL)

Genotype	Planned relative time	n	Mean	SD
Deletion	Baseline *	20	0.79997	0.331749
	Follow-up	21	0.68500	0.295952
Duplication	Baseline *	11	0.80123	0.287341
	Follow-up	11	0.80173	0.244761
Other	Baseline *	7	0.55514	0.197107
	Follow-up	6	0.74200	0.303641

Tetranor-PGDM (ng/mL)

Genotype	Planned relative time	n	Mean	SD
Deletion	Baseline *	20	2.17119	1.747841
	Follow-up	21	1.83590	1.142444
Duplication	Baseline *	11	1.63200	0.575813
	Follow-up	11	1.55835	0.529080
Other	Baseline *	7	1.48963	0.478358
	Follow-up	6	1.64677	0.413274

Tetranor-PGEM (ng/mL)

Genotype	Planned relative time	n	Mean	SD
Deletion	Baseline *	20	18.66535	17.137486
	Follow-up	21	16.20019	10.487704
Duplication	Baseline *	11	14.67973	11.007155
	Follow-up	11	12.50773	6.475147
Other	Baseline *	7	10.25400	2.609440
	Follow-up	6	16.69067	6.803690

Urine Osmolality (mmol/kg)

Genotype	Planned relative time	n	Mean	SD
Deletion	Baseline *	21	889.57	186.192
	Follow-up	20	928.85	208.834
Duplication	Baseline *	11	792.86	175.453
	Follow-up	11	909.64	206.579
Other	Baseline *	7	824.43	147.239
	Follow-up	6	898.00	182.170

*: Baseline is the mean of Day 1 and Week 2.

Conclusions: Elevated concentrations of creatinine-corrected urinary PGDM were noted in subjects with DMD compared with HV. Concentrations of uncorrected urinary PGDM was numerically greater in subjects with DMD compared to HV, while concentrations of urinary creatinine were numerically lower in subjects with DMD compared to HV.

When corrected for osmolality, the adjusted mean levels of PGDM and PGEM were numerically higher in subjects with DMD in most age groups, but the confidence intervals for the difference did not exclude zero.

Among subjects with DMD, the levels of PGDM and PGEM corrected for creatinine and osmolality were numerically higher in the oldest age group of 12-16 years compared with the younger age groups; however, no age-specific trend was observed with any of the uncorrected biomarkers.

No meaningful differences from Baseline were observed at the 12-month Follow-up in any of the urine biomarkers.

No correlation between urine osmolality and PGDM levels was observed.

Levels of PGDM and PGEM corrected for creatinine were higher in the non-ambulatory subjects (Stages 4/5) compared with ambulatory subjects (Stages 1/2) at both Baseline and Follow-up. This trend was less prominent in the levels of PGDM and PGEM corrected for osmolality. Creatinine levels were lowest in the late non-ambulatory subjects (Stage 5).

The change from Baseline in the levels of both PGDM and PGEM (corrected for creatinine and osmolality) was similar between subjects who experienced a worsening in ambulatory status and those who experienced no change.

Baseline levels of corrected PGDM and PGEM were generally higher in subjects who were non-ambulatory (Stages 4/5) at Follow up compared with those who were ambulatory (Stages 2/3). No specific differences were observed in the levels of other biomarkers except that the Baseline creatinine levels and osmolality were lowest in late non-ambulatory subjects (Stage 5) at the 12-month Follow-up.

Baseline levels of PGDM and PGEM corrected for creatinine were slightly higher in subjects who experienced a worsening in ambulatory status as compared with those who experienced no change at the 12-month Follow-up. No such differences were observed in the levels of PGDM and PGEM corrected for osmolality.

No meaningful differences were observed in the distribution of biomarker levels among the 3 types of mutations.