

Supplementary Table 8. Analysis of Biomarkers of Exposure – THS and Cigarette Smoking arm – As Randomized.

Biomarker of Exposure	Time Point	LS Means (95% CI)		LS Means Ratio / Difference** (95% CI)
		THS	Cigarette Smoking	THS vs. Cigarettes
MHBMA (pg/mg creat.)	Baseline*	1887 (1678 ; 2121)	2057 (1846 ; 2292)	----
	Month 3	1275 (1126 ; 1444)	1982 (1754 ; 2239)	64.3 (57.2 ; 72.4)
	Month 6	1341 (1175 ; 1531)	1996 (1754 ; 2271)	67.2 (58.7 ; 76.9)
3-HPMA (ng/mg creat.)	Baseline*	1302 (1216 ; 1394)	1328 (1245 ; 1416)	----
	Month 3	997 (938 ; 1059)	1308 (1234 ; 1388)	76.2 (70.4 ; 82.4)
	Month 6	1044 (977 ; 1116)	1277 (1198 ; 1361)	81.8 (75.0 ; 89.2)
Total NNN (pg/mg creat.)	Baseline*	9.64 (8.55 ; 10.9)	10.7 (9.53 ; 12.1)	----
	Month 3	6.23 (5.33 ; 7.27)	8.23 (7.07 ; 9.59)	75.6 (64.7 ; 88.4)
	Month 6	6.17 (5.27 ; 7.23)	8.64 (7.40 ; 10.1)	71.5 (60.9 ; 83.9)
CEMA (ng/mg creat.)	Baseline*	167 (154 ; 181)	170 (157 ; 184)	----
	Month 3	105 (94.7 ; 117)	172 (155 ; 190)	61.3 (54.7 ; 68.8)
	Month 6	104 (92.3 ; 117)	160 (143 ; 180)	64.8 (56.4 ; 74.4)
3-OH-B[a]P (fg/mg creat.)	Baseline*	161 (151 ; 173)	161 (151 ; 173)	----
	Month 3	130 (117 ; 144)	161 (146 ; 178)	80.5 (73.9 ; 87.8)
	Month 6	129 (116 ; 143)	160 (145 ; 177)	80.6 (73.4 ; 88.5)
3-HMPMA (ng/mg creat.)	Baseline*	311 (291 ; 332)	321 (300 ; 342)	----
	Month 3	232 (215 ; 251)	312 (289 ; 337)	74.3 (68.2 ; 81.0)
	Month 6	245 (227 ; 266)	307 (284 ; 332)	79.9 (73.2 ; 87.3)
Total 1-OHP (pg/mg creat.)	Baseline*	290 (273 ; 309)	284 (266 ; 302)	----
	Month 3	246 (226 ; 268)	288 (265 ; 313)	85.5 (78.5 ; 93.1)
	Month 6	244 (224 ; 267)	278 (255 ; 303)	88.0 (80.2 ; 96.5)
Neq (mg/g creat.)	Baseline*	9.66 (9.02 ; 10.3)	10.2 (9.52 ; 10.8)	----
	Month 3	9.09 (8.62 ; 9.59)	9.44 (8.97 ; 9.94)	96.3 (89.9 ; 103)
	Month 6	8.73 (8.19 ; 9.30)	8.82 (8.30 ; 9.37)	99.0 (91.1 ; 108)
CO exhaled (ppm)	Baseline*	23.0 (21.7 ; 24.4)	23.9 (22.5 ; 25.2)	----
	Month 3	17.0 (15.2 ; 18.9)	20.8 (19.0 ; 22.6)	-3.79 (-5.28 ; -2.30)
	Month 6	18.1 (14.6 ; 21.6)	24.3 (21.0 ; 27.6)	-6.21 (-10.6 ; -1.82)

* Geometric Means in case of Baseline of MHBMA, 3-HPMA, Total NNN, CEMA, 3-OH-B[a]P, HMPMA, Total 1-OHP, Neq, ordinary means in case of CO exhaled.

** LS Mean Ratios in case of MHBMA, 3-HPMA, Total NNN, CEMA, 3-OH-B[a]P, 3-HMPMA, Total 1-OHP, Neq.

LS Mean Differences in case of CO exhaled.

MHBMA = monohydroxybutenylmercapturic acid; 3-HPMA = 3-hydroxypropylmercapturic acid, Total NNN = total N-nitrosomonocotine, CEMA = 2-cyanoethylmercapturic acid, 3-OH-B[a]P = 3-hydroxybenzo(a)pyrene, 3-HMPMA = 3-hydroxy-1-methylpropylmercapturic acid, Total 1-OHP = total 1-hydroxypyrene, Neq = nicotine equivalents, CO exhaled = carbon monoxide exhaled.