Supplementary table 10. Differences in *FKBP5* methylation according to practitioner’s decision to adjust therapy

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Under-replacement**  **(n=4)** | **Appropriate replacement**  **(n=52)** | **Over-replacement**  **(n=13)** | **p** |
| **Sex** |  |  |  |  |
| Male, n (%) | 1 (25) | 16 (31) | 2 (15) | 0.54 |
| Female, n (%) | 3 (75) | 36 (69) | 11 (85) |
| **AI etiology** |  |  |  |  |
| Primary, n (%) | 3 (75) | 33 (64) | 10 (77) | 0.19 |
| Secondary, (%) | 1 (25) | 19 (36) | 3 (23) |
| **Hydrocortisone replacement dose** |  |  |  |  |
| mg/day | 19 ± 3 | 21 ± 7 | 26 ± 7 | 0.08 |
| mg/BSA/day | 11 ± 3 | 11 ± 4 | 13 ± 5 | 0.33 |
| **FKBP5 methylation, %,**  **mean ± SD** |  |  |  |  |
| Intron1A1 CpG185 | 19 ± 4 | 20 ± 8 | 16 ± 9 | 0.92 |
| Intron1A1 CpG189 | 39 ± 4 | 36 ± 9 | 34 ± 12 | 0.95 |
| Intron1A2 CpG49 | 97 ± 2 | 96 ± 2 | 96 ± 2 | 1.00 |
| Intron1A2 CpG126 | 94 ± 2 | 94 ± 1 | 94 ± 1 | 1.10 |
| Intron1A2 CpG143 | 98 ± 1 | 97 ± 1 | 98 ± 1 | 0.86 |
| Intron1A2 CpG190 | 98 ± 1 | 97 ± 1 | 97 ± 1 | 0.94 |
| Intron2A1 CpG62 | 93 ± 3 | 92 ± 3 | 91 ± 2 | 0.96 |
| Intron2A1 CpG115 | 92 ± 8 | 95 ± 2 | 94 ± 1 | 0.92 |
| Intron2A1 CpG180 | 97 ± 1 | 96 ± 1 | 96 ± 1 | 1.04 |
| Intron2A1 CpG228 | 94 ± 2 | 92 ± 2 | 92 ± 2 | 0.97 |
| Intron5A1 CpG97 | 1.8 ± 1 | 1.7 ± 1 | 1.7 ± 1 | 1.05 |
| Intron5A1 CpG123 | 1 ± 0.6 | 0.9 ± 0.5 | 1 ± 0.6 | 1.07 |
| Intron5A1 CpG242 | 1.3 ± 0.6 | 1.7 ± 1 | 1.8 ± 0.9 | 0.96 |
| Intron5A1 CpG262 | 1.5 ± 0.6 | 1.7 ± 1 | 2.6 ± 2 | 0.92 |
| Intron5A1 CpG268 | 1.6 ± 0.5 | 1.8 ± 1 | 1.7 ± 1 | 1.13 |
| Intron5A2 CpG66 | 92 ± 3 | 91 ± 2 | 91 ± 2 | 0.90 |
| Intron5A2 CpG127 | 98 ± 0.3 | 97 ± 1 | 98 ± 1 | 0.44 |
| Intron5A2 CpG218 | 97 ± 2 | 96 ± 2 | 95 ± 2 | 0.90 |
| Intron5A3 CpG133 | 7 ± 4 | 8 ± 3 | 8 ± 3 | 1.04 |
| Intron7A1 CpG127 | 61 ± 4 | 58 ± 7 | 58 ± 5 | 0.95 |
| Intron7A1 CpG138 | 57 ± 4 | 53 ± 6 | 53 ± 5 | 0.92 |
| Intron7A1 CpG282 | 78 ± 4 | 78 ± 6 | 77 ± 5 | 1.01 |
| Intron7A2 CpG41 | 82 ± 4 | 80 ± 5 | 79 ± 3 | 1.04 |
| Intron7A2 CpG94 | 98 ± 0.6 | 96 ± 1 | 96 ± 0.8 | 0.69 |
| Intron7A2 CpG119 | 98 ± 2 | 97 ± 1 | 96 ± 1 | 0.87 |
| Intron7A2 CpG169 | 74 ± 5 | 71 ± 10 | 71 ± 8 | 1.15 |
| Intron7A2 CpG221 | 84 ± 2 | 83 ± 8 | 81 ± 5 | 1.04 |
| PromoterA1 CpG112 | 3 ± 4 | 11 ± 9 | 12 ± 8 | 0.99 |
| PromoterA1 CpG128 | 27 ± 5 | 24 ± 5 | 23 ± 6 | 0.87 |
| PromoterA1 CpG175 | 29 ± 2 | 30 ± 5 | 28 ± 4 | 0.96 |
| PromoterA1 CpG199 | 7 ± 1 | 8 ± 2 | 7 ± 2 | 1.05 |
| PromoterA2 CpG48 | 86 ± 0.2 | 85 ± 2 | 86 ± 2 | 1.06 |
| PromoterA2 CpG89 | 97 ± 2 | 97 ± 1 | 97 ± 0.5 | 1.09 |
| PromoterA2 CpG101 | 97 ± 0.6 | 97 ± 1 | 97 ± 0.8 | 0.99 |
| PromoterA2 CpG168 | 95 ± 3 | 95 ± 2 | 94 ± 2 | 0.93 |
| PromoterA2 CpG215 | 74 ± 2 | 69 ± 4 | 68 ± 4 | 1.08 |
| PromoterA2 CpG253 | 98 ± 1 | 96 ± 1 | 96 ± 1 | 0.77 |
| PromoterA2 CpG288 | 90 ± 4 | 88 ± 3 | 88 ± 3 | 0.97 |
| Proximal EnhancerA1CpG83 | 13 ± 8 | 12 ± 5 | 12 ± 3 | 1.08 |
| Proximal EnhancerA1CpG91 | 12 ± 7 | 12 ± 5 | 11 ±3 | 1.02 |
| Proximal EnhancerA1CpG134 | 3 ± 1 | 3 ± 1 | 3 ± 0.7 | 1.08 |
| Proximal EnhancerA1CpG207 | 22 ± 11 | 20 ± 8 | 19 ± 5 | 1.11 |
| Proximal EnhancerA1CpG216 | 21 ± 11 | 19 ± 8 | 20 ± 5 | 1.04 |
| Proximal EnhancerA1CpG226 | 17 ± 10 | 17 ± 7 | 17 ± 5 | 0.98 |
| Proximal EnhancerA1CpG265 | 24 ± 12 | 23 ± 10 | 23 ± 7 | 0.99 |
| Proximal EnhancerA2 CpG84 | 4 ± 4 | 12 ± 9 | 13 ± 9 | 0.91 |
| Proximal EnhancerA2 CpG100 | 26 ± 6 | 25 ± 6 | 22 ± 6 | 0.94 |
| Proximal EnhancerA2 CpG147 | 28 ± 4 | 29 ± 5 | 28 ± 4 | 0.96 |
| Proximal EnhancerA2 CpG171 | 7 ± 1 | 8 ± 2 | 8 ± 2 | 0.95 |
| Proximal EnhancerA2 CpG244 | 22 ± 5 | 20 ± 4 | 19 ± 4 | 0.98 |
| Proximal EnhancerA3 CpG148 | 2 ± 3 | 12 ± 11 | 13 ± 9 | 1.01 |
| Proximal EnhancerA3 CpG199 | 64 ± 7 | 57 ± 9 | 55 ± 7 | 1.06 |
| Proximal EnhancerA4 CpG191 | 26 ± 4 | 28 ± 5 | 22 ± 8 | 0.70 |
| Proximal EnhancerA4 CpG232 | 44 ± 4 | 41 ± 8 | 39 ± 7 | 0.92 |

AI adrenal insufficiency, BSA body surface area