**Supplementary Table 5. Cyclic GMP responses in rectal biopsies in subjects receiving linaclotide (Active) or placebo**

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| --- | --- | --- |
|  | **Day 1** | **Day 7** |
| **Subject** | **2** | **4** | **5** | **6** | **8** | **9** | **2** | **4** | **5** | **5** | **8** | **9** |
| **Rectum (cGMP ng/mg)** |  |  |  |  |  |  |  |  |  |  |  |  |
| Biopsy site 1-1 | 3.53 | 3.58 | 3.79 | 2.21 | 2.70 | 7.84 | 8.44 | 10.13 | 4.32 | 2.57 | 2.29 | 6.03 |
| Biopsy site 1-2 | 3.77 | 4.51 | 3.46 | 2.38 | 2.88 | 6.82 | 8.01 | 10.43 | 4.52 | 2.58 | 2.43 | 6.20 |
| Biopsy site 1-3 | 3.96 | 3.18 | 4.05 | 2.19 | 2.31 | 7.98 | 6.97 | 12.06 | 3.54 | 2.27 | 2.21 | 7.97 |
| Biopsy site 2-1 | 2.67 | 3.30 | 2.64 | 3.92 | 3.56 | 5.44 | 14.50 | 5.66 | 4.66 | 4.75 | 4.83 | 10.26 |
| Biopsy site 2-2 | 2.81 | 3.25 | 3.21 | 3.38 | 4.37 | 5.03 | 12.28 | 5.19 | 5.35 | 4.46 | 4.89 | 9.58 |
| Biopsy site 2-3 | 3.08 | 3.25 | 4.79 | 3.98 | 3.86 | 4.89 | 20.87 | 5.56 | 4.97 | 4.01 | 4.77 | 8.44 |
| **Analysis across both sites combined (per protocol)** |  |  |  |  |  |  |  |  |  |  |  |  |
| **Mean** | 3.30 | 3.51 | 3.66 | 3.01 | 3.28 | 6.33 | 11.85 | 8.17 | 4.56 | 3.44 | 3.57 | 8.09 |
| **Baseline variance** | 0.28 | 0.26 | 0.55 | 0.73 | 0.61 | 1.96 |  |  |  |  |  |  |
| **Baseline pooled variance** | 0.73 |  |  |  |  |  |  |  |  |  |  |  |
| **Baseline pooled standard deviation** | 0.85 |  |  |  |  |  |  |  |  |  |  |  |
| **Delta (Pharmacological effect)** |  |  |  |  |  |  | 8.54 | 4.66 | 0.90 | 0.43 | 0.29 | 1.75 |
| **Delta/pooled baseline SD (PD Effect)** |  |  |  |  |  |  | **10.00** | **5.46** | 1.05 | 0.50 | 0.34 | 2.05 |
| **Pharmacodynamic (PD) Response (PD Effect ≥ 0.94)** |  |  |  |  |  |  | Yes | Yes | Yes | No | No | Yes |
| **Treatment arm** |  |  |  |  |  |  | Active | Active | Placebo | Placebo | Active | Placebo |