**Supplementary Table 3. Cyclic GMP responses in cecal biopsies in subjects receiving linaclotide (Active) or placebo**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Day 1** | | | | | | **Day 7** | | | | | |
| **Subject** | **2** | **4** | **5** | **6** | **8** | **9** | **2** | **4** | **5** | **5** | **8** | **9** |
| **Cecum (cGMP ng/mg)** |  |  |  |  |  |  |  |  |  |  |  |  |
| Biopsy site 1-1 | 2.67 | 3.50 | 7.62 | 2.32 | 2.43 | 4.97 | 22.30 | 16.94 | 5.53 | 2.19 | 3.26 | 5.14 |
| Biopsy site 1-2 | 3.36 | 4.32 | 6.56 | 2.39 | 2.27 | 4.17 | 23.66 | 16.94 | 5.51 | 2.10 | 3.32 | 5.30 |
| Biopsy site 1-3 | 2.69 | 3.76 | 7.06 | 2.38 | 1.93 | 4.67 | 23.89 | 25.82 | 5.22 | 2.11 | 2.98 | 5.89 |
| Biopsy site 2-1 | 3.35 | 0.71 | 1.81 | 4.93 | 3.64 | 6.45 | 6.06 | 2.71 | 1.09 | 2.90 | 4.08 | 17.16 |
| Biopsy site 2-2 | 3.33 | 0.75 | 2.34 | 4.59 | 2.78 | 6.89 | 6.96 | 28.77 | 0.74 | 2.81 | 5.24 | 19.27 |
| Biopsy site 2-3 | 3.10 | 0.69 | 2.45 | 4.50 | 3.12 | 6.45 | 7.05 | 9.58 | 0.79 | 3.27 | 3.28 | 18.87 |
| **Analysis across both biopsy sites combined (per protocol)** |  |  |  |  |  |  |  |  |  |  |  |  |
| **Mean** | 3.22 | 2.29 | 4.64 | 3.52 | 2.69 | 5.60 | 15.32 | 16.79 | 3.15 | 2.56 | 3.69 | 11.94 |
| **Baseline variance** | 0.22 | 3.04 | 7.32 | 1.62 | 0.38 | 1.28 |  |  |  |  |  |  |
| **Baseline pooled variance** | 2.31 |  |  |  |  |  |  |  |  |  |  |  |
| **Baseline pooled standard deviation** | 1.52 |  |  |  |  |  |  |  |  |  |  |  |
| **Delta (Pharmacological effect)** |  |  |  |  |  |  | 12.10 | 14.50 | -1.49 | -0.96 | 1.00 | 6.34 |
| **Delta/pooled baseline SD (PD Effect)** |  |  |  |  |  |  | **7.97** | **9.55** | -0.98 | -0.63 | 0.66 | 4.17 |
| **Pharmacodynamic (PD) Response  (PD Effect ≥ 0.94)** |  |  |  |  |  |  | Yes | Yes | No | No | No | Yes |
| **Treatment arm** |  |  |  |  |  |  | Active | Active | Placebo | Placebo | Active | Placebo |