**Supplementary Table 4. Cyclic GMP responses in transverse colon 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** |
| **Transverse colon (cGMP ng/mg)** |  |  | |  | | |  | |  | |  | |  |  | |  |  |  |  |
| Biopsy site 1-1 | 1.68 | 5.03 | | 13.56 | | | 3.62 | | 3.67 | | 5.49 | | 12.03 | 17.92 | 7.57 | | 2.22 | 2.25 | 7.53 |
| Biopsy site 1-2 | 2.14 | 4.79 | | 13.29 | | | 3.25 | | 3.38 | | 4.91 | | 12.69 | 25.12 | 6.06 | | 2.29 | 2.40 | 6.01 |
| Biopsy site 1-3 | 1.12 | 4.70 | | 14.25 | | | 4.25 | | 2.92 | | 4.72 | | 11.98 | 29.99 | 6.87 | | 2.09 | 2.16 | 5.75 |
| Biopsy site 2-1 | 4.65 | 3.93 | | 0.60 | | | 4.99 | | 4.47 | | 10.62 | | 7.15 | 23.55 | 3.14 | | 5.59 | 5.31 | 6.46 |
| Biopsy site 2-2 | 5.25 | 4.06 | | 0.64 | | | 5.44 | | 4.47 | | 11.02 | | 6.15 | 14.91 | 3.13 | | 5.26 | 5.09 | 7.06 |
| Biopsy site 2-3 | 3.12 | 4.21 | | 0.66 | | | 5.02 | | 3.95 | | 11.59 | | 8.19 | 15.90 | 3.75 | | 5.01 | 4.20 | 3.48 |
| **Analysis across both biopsy sites combined (per protocol)** |  |  | |  | | |  | |  | |  | |  |  |  | |  |  |  |
| **Mean** | 2.91 | 4.45 | | 7.17 | | | 4.43 | | 3.84 | | 8.06 | | 9.70 | 21.23 | 5.09 | | 3.75 | 3.57 | 6.05 |
| **Baseline variance** | 3.08 | 0.20 | | 51.35 | | | 0.75 | | 0.44 | | 11.09 | | 8.19 | 35.29 | 3.91 | | 2.89 | 2.17 | 2.02 |
| **Baseline pooled variance** | 11.15 |  | |  | | |  | | |  | |  |  |  |  | |  |  |  |
| **Baseline pooled standard deviation** | 3.34 |  | |  | | |  | | |  | |  |  |  |  | |  |  |  |
| **Delta (Pharmacological effect)** |  | |  | | |  | |  | |  | |  | 6.79 | 16.78 | -2.07 | | -0.68 | -0.28 | -2.01 |
| **Delta/pooled baseline SD (PD Effect)** |  | |  | | |  | |  | |  | |  | **2.04** | **5.02** | -0.62 | | -0.20 | -0.08 | -0.60 |
| **Pharmacodynamic (PD) Response  (PD Effect ≥ 0.94)** |  | |  | | |  | |  | |  | |  | Yes | Yes | No | | No | No | No |
| **Treatment arm** |  | |  | |  | | |  | |  | |  | Active | Active | Placebo | | Placebo | Active | Placebo |