**Supplemental Table 1: Multivariable and bivariable analyses evaluating the impact of age, gender, suspicion of IBS, management by gastroenterology, and choice of therapy on the hazard of discontinuing IBS-C/CIC therapy (reported in odds ratios with 95% confidence intervals)**

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|  | **Combined multivariate model (n=1,612)** | **Bivariate analyses** |
| **Lubiprostone cohort (n=933)** | **Linaclotide cohort (n=679)** | **Combined cohort (n=1,612)** |
| *Discontinuation for any reason* |
| Therapy with linaclotide(reference therapy = lubiprostone) | **0.644 (0.540 to 0.768) [p<0.001]** | N/A | **0.598 (0.511 to 0.699) [p<0.001]** |
| Age (years) | 1.003 (0.999 to 1.008) | 0.998 (0.992 to 1.004) | **1.010 (1.002 to 1.017) [p=0.01]** | 1.002 (0.997 to 1.007) |
| Female | 0.964 (0.778 to 1.195) | 1.017 (0.755 to 1.369) | 0.902 (0.666 to 1.223) | 0.996 (0.806 to 1.231) |
| High suspicion for IBS | **1.361 (1.143 to 1.620) [p=0.001]** | **1.527 (1.205 to 1.935) [p<0.001]** | **1.308 (1.015 to 1.684) [p=0.04]** | **1.658 (1.422 to 1.934) [p<0.001]** |
| Managed by gastroenterology | 1.378 (0.983 to 1.932) p=0.06 | **1.831 (1.090 to 3.076) [p=0.01]** | 1.065 (0.682 to 1.663) | **1.436 (1.025 to 2.011) [p=0.03]** |
| *Discontinuation due to intolerance* |
| Therapy with linaclotide(reference therapy = lubiprostone) | **1.926 (1.442 to 2.574) [p<0.001]** | N/A | **1.796 (1.379 to 2.339) [p<0.001]** |
| Age (years) | 1.006 (0.998 to 1.014) | 1.005 (0.993 to 1.018) | 1.005 (0.996 to 1.014) | 1.005 (0.998 to 1.013) |
| Female | 1.197 (0.836 to 1.714) | 1.649 (0.760 to 3.579) | 1.107 (0.740 to 1.657) | 1.188 (0.832 to 1.695) |
| High suspicion for IBS | **1.311 (1.003 to 1.714) [p=0.047]** | 1.525 (0.901 to 2.581) | 1.302 (0.953 to 1.780) | 1.059 (0.831 to 1.348) |
| Initiated by gastroenterology | 1.441 (0.839 to 2.479) | 1.751 (0.551 to 5.561) | 1.365 (0.742 to 2.511) | 1.441 (0.841 to 2.470) |
| *Discontinuation due to therapy ineffectiveness* |
| Therapy with linaclotide(reference therapy = lubiprostone) | **0.565 (0.412 to 0.775) [p<0.001]** | N/A | **0.520 (0.392 to 0.690) [p<0.001]** |
| Age (years) | **1.010 (1.002 to 1.019) [p=0.02]** | 1.001 (0.991 to 1.011) | **1.026 (1.011 to 1.040) [p<0.001]** | **1.009 (1.001 to 1.018) [p=0.03]** |
| Female | 1.020 (0.687 to 1.513) | 1.461 (0.807 to 2.648) | 0.694 (0.410 to 1.173) | 1.049 (0.712 to 1.544) |
| High suspicion for IBS | **1.501 (1.098 to 2.053) [p=0.01]** | **1.747 (1.144 to 2.666) [p<0.001]** | 1.392 (0.873 to 2.221) | 1.902 (1.440 to 2.513) |
| Initiated by gastroenterology | 2.012 (0.989 to 4.092) [p=0.054] | **3.196 (1.013 to 10.079) [p=0.02]** | 1.284 (0.519 to 3.179) | **2.079 (1.024 to 4.222) [p=0.02]** |

**Supplement Table 2. Comparison of baseline demographics between patients who did or did not discontinue lubiprostone or linaclotide within three months or one year of initiating therapy**

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| Characteristic |  |  | p-value |
|  | Discontinuation within 3 months (n=285) | Continuing beyond 3 months (n=1,327) |  |
| Age | 49.9 years (SD=18.5) | 49.2 years (SD=16.7) | p=0.51 |
| Female | 229/285 (80.4%) | 1,117/1,327 (84.2%) | p=0.12 |
| High suspicion of IBS (based on ICD-9 coding) | 552/1,327 (41.6%) | 165/285 (57.9%) | p<0.001 |
| Managed by gastroenterology | 263/285 (93.6%) | 1,157/1,327 (92.7%) | p=0.60 |
|  | Discontinuation within one year (n=516) | Continuing beyond one year (n=1,096) |  |
| Age | 50.0 years (SD=18.0) | 49.1 years (SD=16.5) | p=0.31 |
| Female | 427/516 (82.8%) | 919/1,096 (83.9%) | p=0.58 |
| High suspicion of IBS (based on ICD-9 coding) | 293/516 (56.8%) | 424/1,096 (38.7%) | p<0.001 |
| Managed by gastroenterology | 479/508 (94.2%) | 941/1,021 (92.2%) | p=0.13 |

IBS = irritable bowel syndrome, ICD = World Health Organization International Classification of Diseases, SD = standard deviation