**SUPPLEMENTARY MATERIALS**

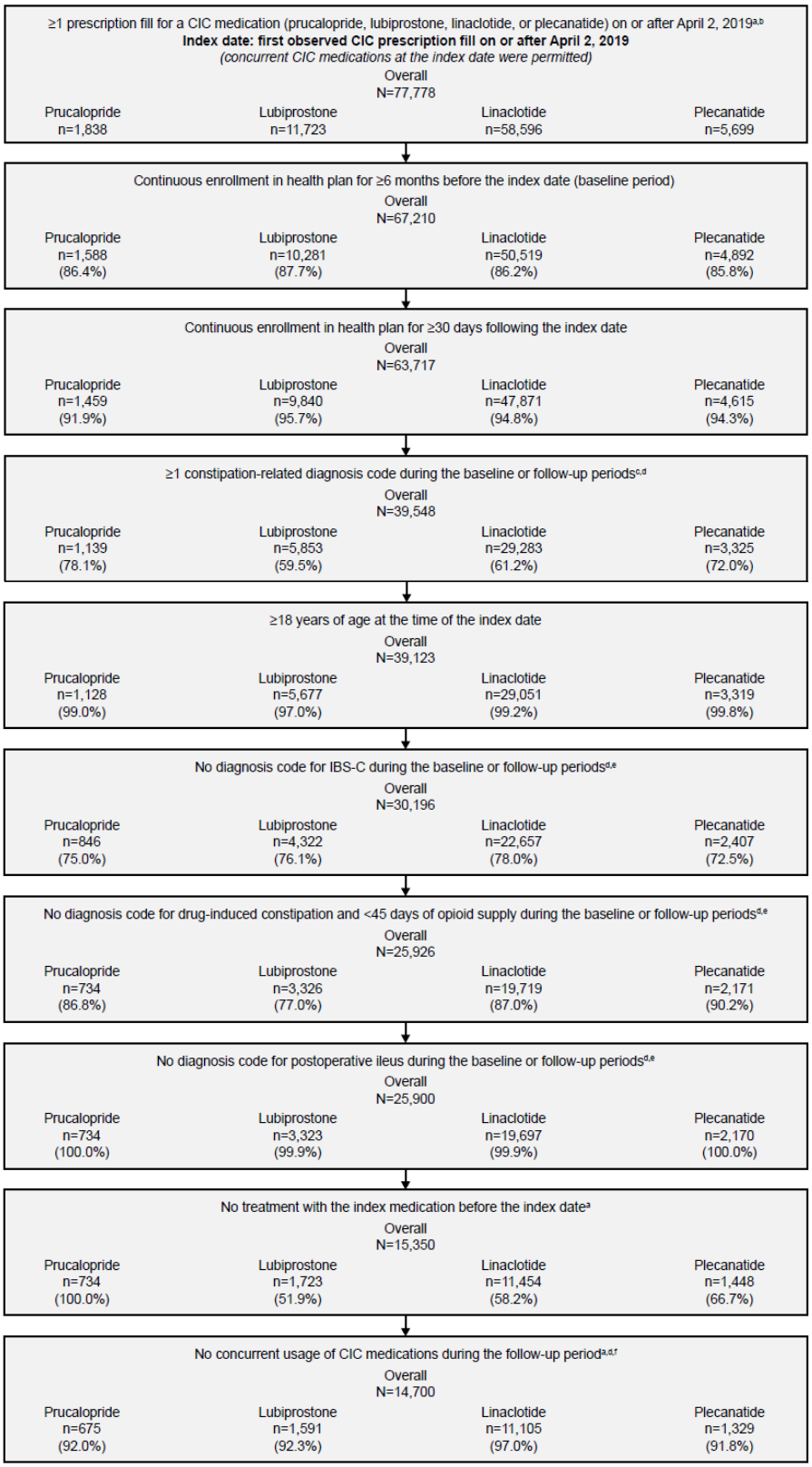
# A real-world study of persistence and adherence to prescription medications in patients with chronic idiopathic constipation in the United States

**Short title:** Patient persistence and adherence to CIC prescription medications

Brooks D. Cash, MD; Mei Lu, MD; Anthony Lembo, MD; Paul Feuerstadt, MD; Linda Nguyen, MD; Emi Terasawa, PhD; Rajeev Ayyagari, PhD; Shawn Du, PhD; Selina Pi, BSE; Ben Westermeyer, BA; Brian Terreri, PharmD; Mena Boules, MD; Baharak Moshiree, MD, MSc

## Supplementary Figures

### Supplementary Figure 1 Participant Selection Algorithm for Patients Who Were Receiving Prucalopride, Lubiprostone, Linaclotide, or Plecanatide for Comparative Analysis



[a]See Supplementary Table 1 for the National Drug Codes used to identify prucalopride, lubiprostone, linaclotide, and plecanatide prescription fills.

[b]Before the final step in the flowchart (in which patients with concurrent usage of constipation medications [prucalopride, lubiprostone, linaclotide, or plecanatide] during the follow-up period were excluded), some patients may have been included in more than one index treatment group. This occurred if a patient used more than one constipation medication (prucalopride, lubiprostone, linaclotide, or plecanatide) on the index date. As a result, the overall sample counts may not equal the sum of the index treatment sample counts before the final step.

[c]See Supplementary Table 2 for ICD-10-CM codes used to identify constipation-related diagnoses.

[d]The follow-up period was defined as the period from the index date to the end of continuous eligibility.

[e]See Supplementary Table 3 for ICD-10-CM and GPI codes used to identify irritable bowel syndrome with constipation, drug-induced constipation, opioid use, and postoperative ileus.

[f]Concurrent usage is defined as having an overlap in days supply of a constipation medication (prucalopride, lubiprostone, linaclotide, or plecanatide) with the index treatment for at least one day during the follow-up period.

CIC=chronic idiopathic constipation; GPI=Generic Product Identifier; IBS-C=irritable bowel syndrome with constipation; ICD-10-CM=International Classification of Diseases, Tenth Revision, Clinical Modification.

**Supplementary Tables**

**Supplementary Table 1 National drug codes for treatments of interest**

| **Treatment generic name** | **NDC** |
|---|---|
| Prucalopride | 54092054601, 54092054701, 54092054702, 54092054703 |
| Lubiprostone | 00254302802, 00254302902, 16590047128, 16590047130, 16590047160, 16590047172, 16590047190, 16590062230, 16590062260, 16590062262, 16590062290, 35356050060, 47463010660, 54868597100, 54868615300, 55048010660, 63629459801, 63629639801, 64764008060, 64764024010, 64764024060, 68151500306 |
| Linaclotide | 00456120104, 00456120130, 00456120204, 00456120230, 00456120304, 00456120330, 55700040930 |
| Plecanatide | 65649000301, 65649000303, 65649000307, 65649000330, 70194000330, 70194010307 |

NDC=National Drug Code.

**Supplementary Table 2 ICD-10-CM constipation-related diagnosis codes used for inclusion criteria**

| **Diagnosis** | **Diagnosis code** |
|---|---|
| Unspecified constipation | K59.00 |
| Slow transit constipation | K59.01 |
| Outlet dysfunction constipation | K59.02 |
| Chronic idiopathic constipation | K59.04 |
| Other constipation | K59.09 |

ICD-10-CM=International Classification of Diseases, Tenth Revision, Clinical Modification.

**Supplementary Table 3 Diagnosis, procedure, and drug codes for exclusion criteria**

| Subject | ICD-10-CM | HCPCS | GPI |
|---|---|---|---|
| Irritable bowel syndrome with constipation | K58.1 | – | – |
| Mixed irritable bowel syndrome | K58.2 | – | – |
| Irritable bowel syndrome without diarrhea | K58.9 | – | – |
| Drug-induced constipation | K59.03 | – | – |
| Opioids | – | J0745, J2270, J2271, J2275, S0093, J3010, J1170, S0092, J1960, J2175, J2180, J1230, S0109, J2140, J0592, J0595, S0009, S0012, J2300, J3070, J0570, J0571, J0572, J0573, J0574, J0575, Q9991, Q9992, Q0167, Q0168 | 65x |
| Postprocedural intestinal obstruction | K91.3x | – | – |

GPI=Generic Product Identifier; HCPCS=Healthcare Common Procedure Coding System; ICD-10-CM=International Classification of Diseases, Tenth Revision, Clinical Modification.

**Supplementary Table 4 Summary of tablet strengths at the index date**

| Tablet strength, n (%) | Prucalopride (n=675) | Lubiprostone (n=1,591) | Linaclotide (n=11,105) | Plecanatide (n=1,329) | All patients (N=14,700) |
|---|---|---|---|---|---|
| Prucalopride | | | | | |
| 1 mg | 90 (13.3) | – | – | – | 90 (0.6) |
| 2 mg | 585 (86.7) | – | – | – | 585 (4.0) |
| Lubiprostone | | | | | |
| 8 µg | – | 651 (40.9) | – | – | 651 (4.4) |
| 24 µg | – | 940 (59.1) | – | – | 940 (6.4) |
| Linaclotide | | | | | |
| 72 µg | – | – | 3,376 (30.4) | – | 3,376 (23.0) |
| 145 µg | – | – | 5,860 (52.8) | – | 5,860 (39.9) |

| | | | | | |
|---|---|---|---|---|---|
| 290 µg | – | – | 1,865 (16.8) | – | 1,865 (12.7) |
| Multiple | – | – | 4 (<0.1) | – | 4 (<0.1) |
| Plecanatide | | | | | |
| 3 mg | – | – | – | 1,329 (100.0) | 1,329 (9.0) |

**Supplementary Table 5 Adjusted Comparison of PDC ≥80% Across Lubiprostone, Linaclotide, and Plecanatide Relative to Prucalopride During the Follow-Up Period**

| | PDC ≥80%[a] (n=8,833) | | |
|---|---|---|---|
| | **Odds ratio[b]** | **95% CI** | ***P*** |
| Index treatment (reference: prucalopride) | | | |
| Lubiprostone | 0.52 | 0.40-0.69 | <0.001 |
| Linaclotide | 0.73 | 0.58-0.93 | 0.009 |
| Plecanatide | 0.70 | 0.53-0.93 | 0.015 |
| Health care resource use during the baseline period | | | |
| Any constipation-related inpatient visits | 1.00 | 0.63-1.58 | 0.996 |
| Any constipation-related ED visits | 0.86 | 0.69-1.08 | 0.207 |
| Number of gastroenterologist visits | 1.09 | 1.01-1.18 | 0.025 |

| | | | |
|---|---|---|---|
| Number of constipation-related outpatient visits | 1.01 | 0.98-1.03 | 0.566 |
| Treatments during the baseline period | | | |
| Lubiprostone | 1.28 | 0.70-2.33 | 0.426 |
| Linaclotide | 0.95 | 0.54-1.67 | 0.865 |
| Plecanatide | 0.78 | 0.25-2.48 | 0.675 |
| Use of any prescription laxatives | 1.16 | 1.02-1.32 | 0.026 |

Statistical significance set at $P<0.05$.

[a]Evaluated for patients who had continuous enrollment for at least 6 months after the index date. PDC was calculated by dividing the patient's total days of supply of index treatment prescriptions filled during the first 6 months of follow-up by the number of days in a 6-month time frame (182 days). Accounting for stockpiling, any days of supply that fell outside of the first 6 months of follow-up were excluded.

[b]Odds ratios were calculated using logistic regression. An odds ratio greater than 1 for a categorical variable (A vs B) indicates the proportionally higher odds of the outcome occurring in group A compared with group B. An odds ratio greater than 1 for a continuous variable indicates the proportionally higher odds of the outcome occurring for a unit increase in the level of the variable.

ED=emergency department; PDC = proportion of days covered.