# Long-Term Safety and Efficacy of Olanzapine/Samidorphan: Results of a 4-Year Open-Label Study

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# Introduction and Background

- Olanzapine is an effective antipsychotic medication for the treatment of schizophrenia and bipolar I disorder, but its use is limited by weight and metabolic concerns[1-4]
- Olanzapine combined with samidorphan (OLZ/SAM) is approved for the treatment of schizophrenia and bipolar I disorder in adults[5]
- OLZ/SAM provides the established antipsychotic efficacy of olanzapine but with less weight gain[6-8]
- The objective of this study was to evaluate the long-term safety, tolerability, and durability of treatment effect of OLZ/SAM in patients with up to 4 years of open-label treatment experience

OLZ/SAM, olanzapine combined with samidorphan.

**1.** Buchanan RW, et al. *Schizophr Bull*. 2010;36(1):71-93. **2.** Yatham LN, et al. *Bipolar Disord.* 2018;20:97-170. **3.** De Hert M, et al. *Nat Rev Endocrinol*. 2012;8(2):114-126. **4.** Correll CU, et al. *Int J Neuropsychopharmacol*. 2023;26(7):451-464. **5.** Lybalvi [*package insert*]. Waltham, MA: Alkermes, Inc.; 2024. **6.** Potkin SG, et al. *J Clin Psychiatry.* 2020;81(2):19m12769. **7.** Correll CU, et al. *Am J Psychiatry*. 2020;177(12):1168-1178. **8.** Kahn RS, et al. *J Clin Psychiatry*. 2023;84(3):22m14674.

# Transition of Patients From Antecedent Studies Into Long-Term Extension Study

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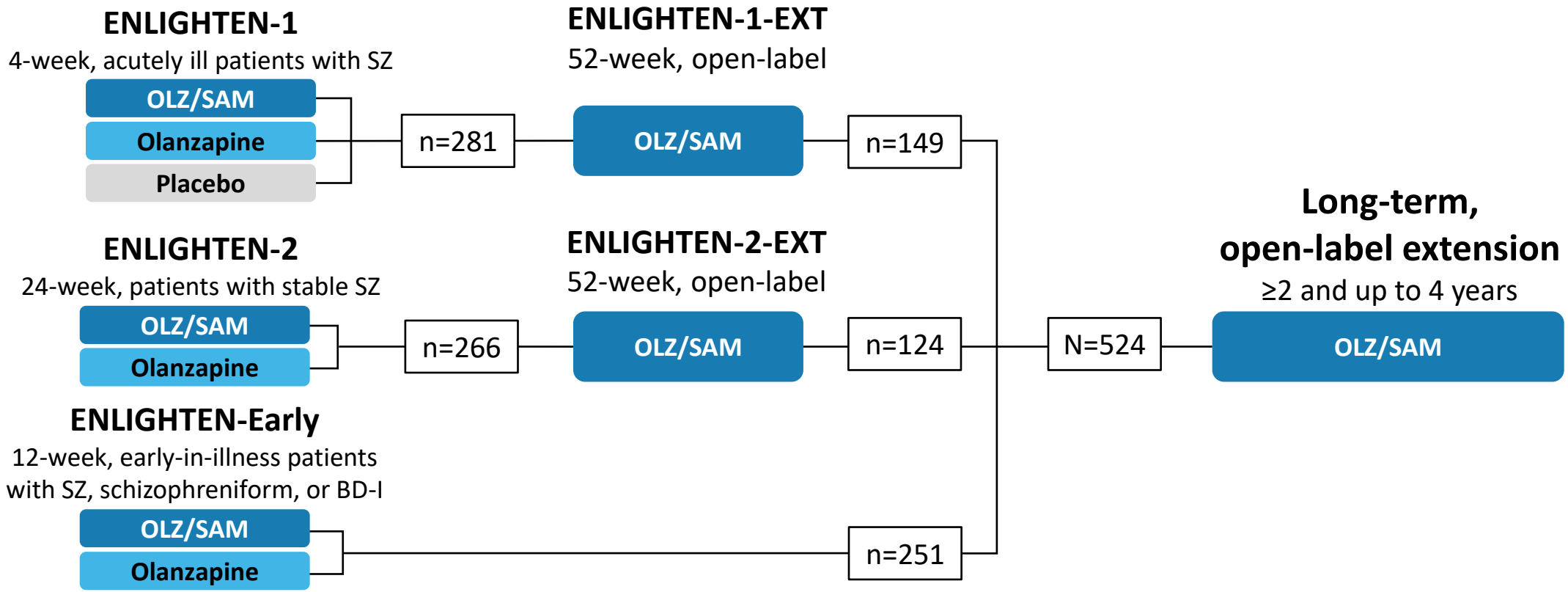


BD-I, bipolar I disorder; EXT, extension; OLZ/SAM, olanzapine combined with samidorphan; SZ, schizophrenia.

# Long-Term Extension Study: Patient Disposition and Sites

Received ≥1 dose[a]
OLZ/SAM
**523**

↓

Completed ≥2 years
OLZ/SAM
**242/451 (53.7%)**

↓

Completed 4 years
OLZ/SAM
**109/335 (32.5%)**

| Reasons for Discontinuation, n (%) | |
|---|---|
| Withdrawal by patient | 133 (25.4) |
| Ukraine-Russia conflict | 72 (13.8) |
| Adverse event | 44 (8.4) |
| Lost to follow-up | 37 (7.1) |
| Other[b] | 20 (3.8) |
| Protocol deviation | 20 (3.8) |
| Not yet determined[c] | 5 (1.0) |

| Participating Countries | Patients, n (%) |
|---|---|
| United States | 206 (39.4) |
| Ukraine | 118 (22.6) |
| Russia | 69 (13.2) |
| Bulgaria | 63 (12.0) |
| Israel | 28 (5.4) |
| Serbia | 25 (4.8) |
| Italy | 4 (0.8) |
| Austria | 2 (0.4) |
| Ireland | 2 (0.4) |
| Poland | 2 (0.4) |
| South Korea | 2 (0.4) |
| United Kingdom | 2 (0.4) |

Study period ran from June 2017 to September 2023.
188/523 (35.9%) of patients met the protocol definition of completion and received at least 2 and up to 4 years of treatment.
[a]The safety population included all patients who enrolled and received ≥1 dose of study drug during the treatment period.
[b]Includes discontinuations due to the COVID-19 pandemic. [c]Reason for treatment discontinuation has not been collected.

# Study Design

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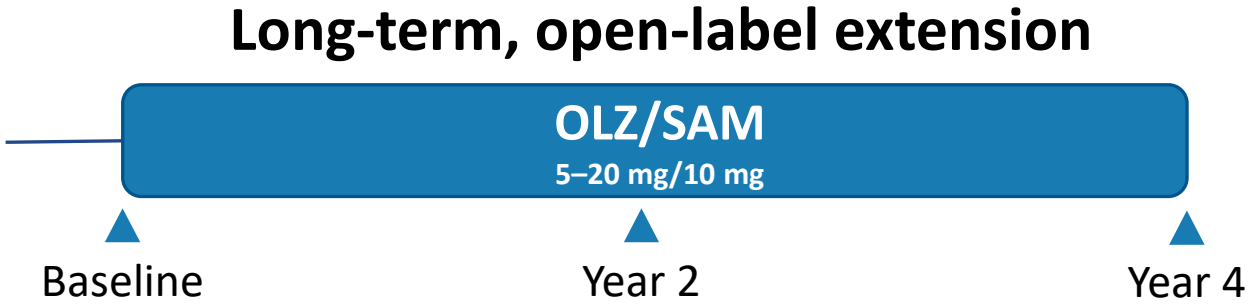



**Key efficacy outcome**

- Change from baseline in CGI-S score

**Key safety outcomes**

- Change from baseline in
  - Body weight
  - Waist circumference
  - Lipid parameters (fasting)
  - Glucose (fasting) and glycosylated hemoglobin
- Incidence and severity of AEs

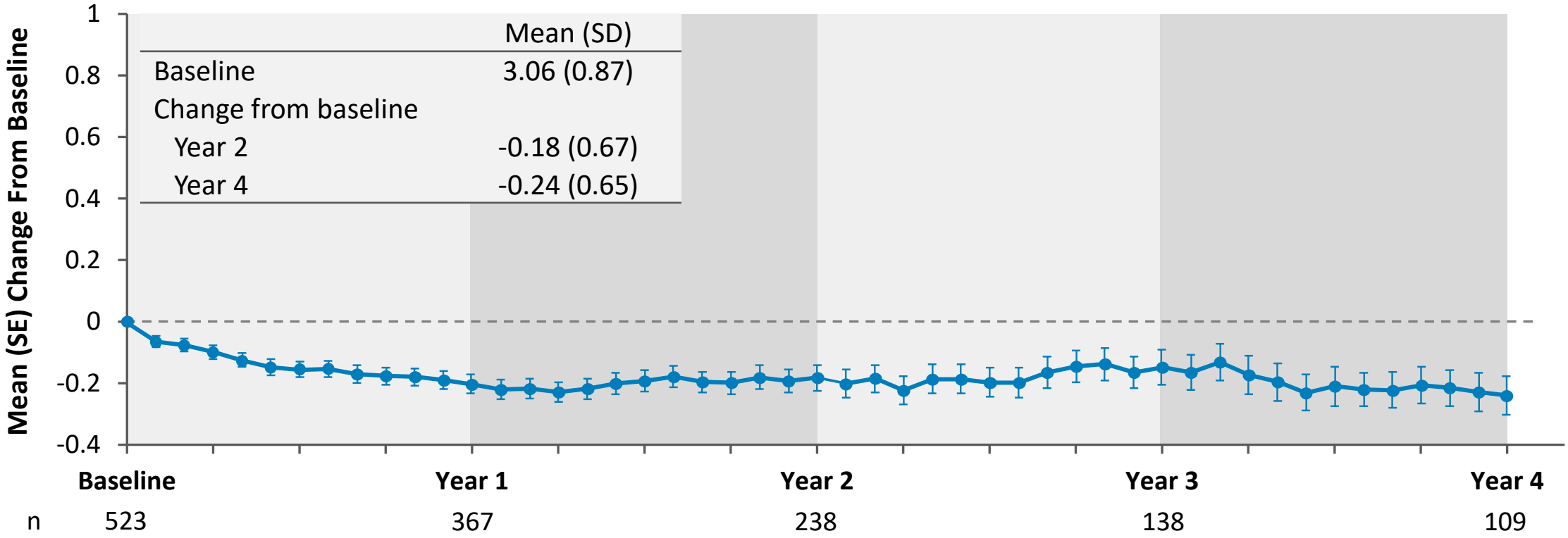
AE, adverse event; CGI-S, Clinical Global Impressions–Severity; OLZ/SAM, olanzapine combined with samidorphan.

# Demographics and Baseline Characteristics

| Parameters | All Patients (N=523) |
|---|---|
| Age, mean (SD), years | 35.1 (12.2) |
| Male, n (%) | 322 (61.6) |
| Race, n (%) | |
| White | 380 (72.7) |
| Black | 126 (24.1) |
| Asian/Other[a] | 17 (3.3) |
| Diagnosis, n (%) | |
| Schizophrenia/schizophreniform disorder | 475 (91.8) |
| Bipolar I disorder | 48 (9.2) |
| Weight, mean (SD), kg | 77.4 (15.5) |
| BMI, mean (SD), kg/m$^2$ | 26.0 (4.3) |
| CGI-S score, mean (SD) | 3.1 (0.9) |

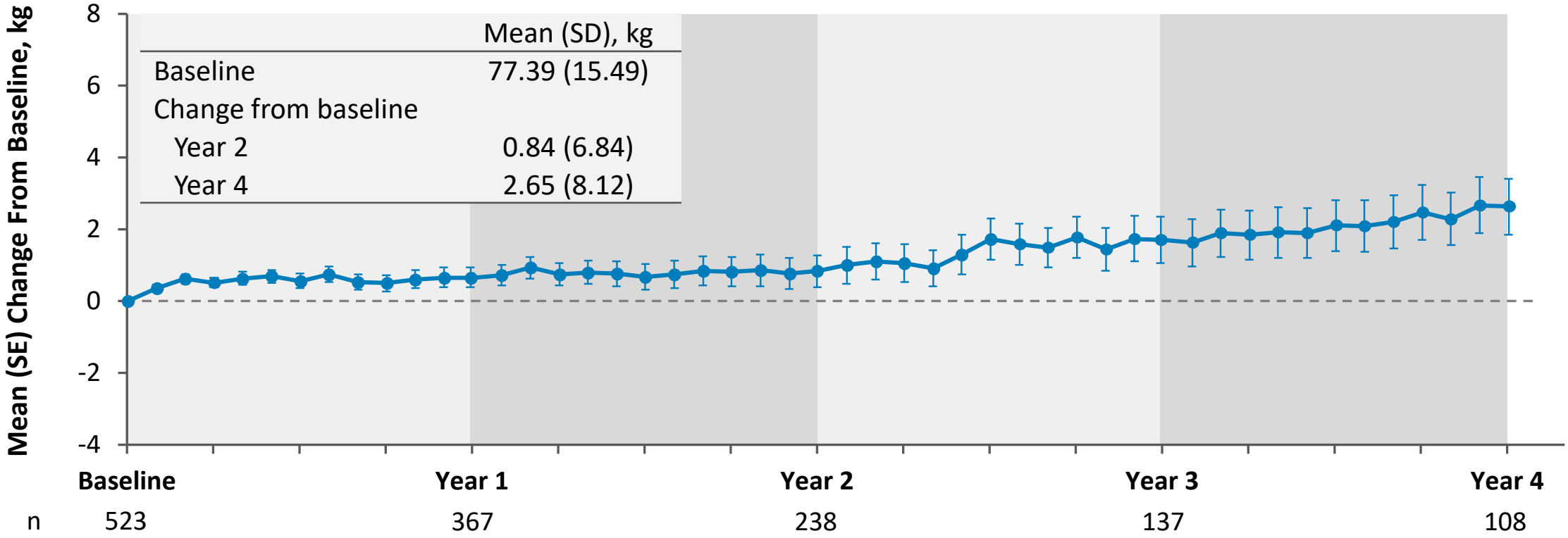
[a]"Other" includes patients who were American Indian or Alaska Native individuals, those reporting multiple races, and those responding "other."
BMI, body mass index; CGI-S, Clinical Global Impressions–Severity.

# Mean Change From Baseline in CGI-S Score

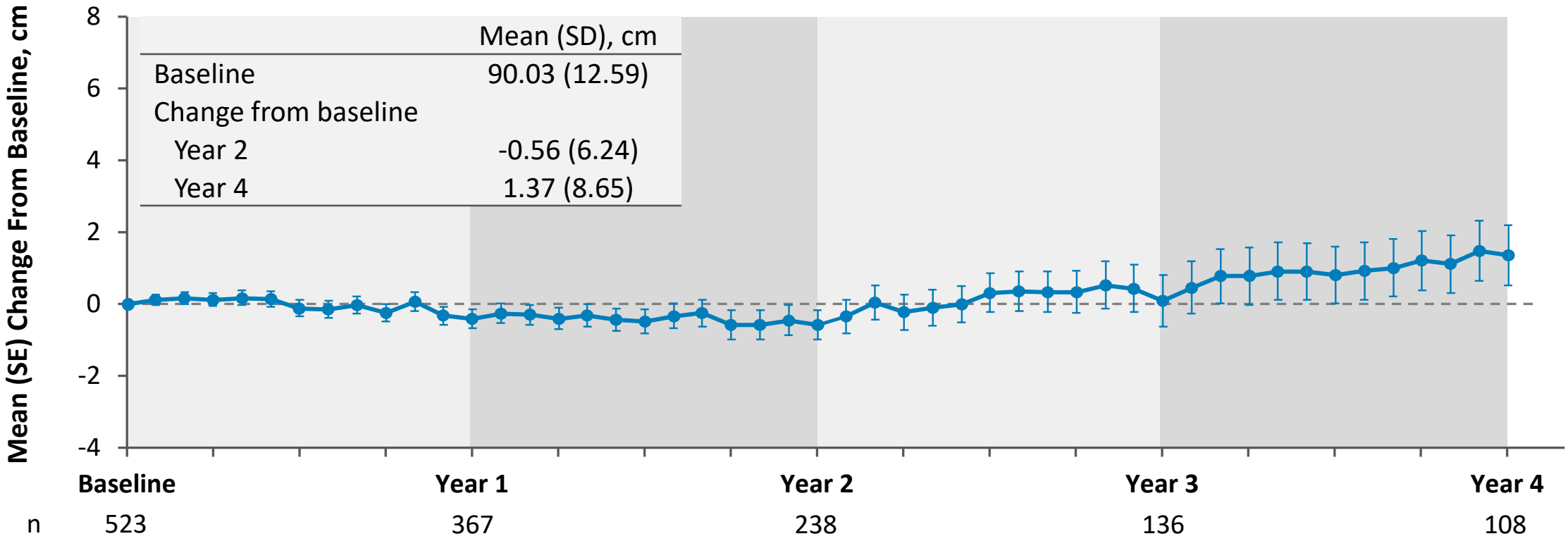



CGI-S, Clinical Global Impressions–Severity.

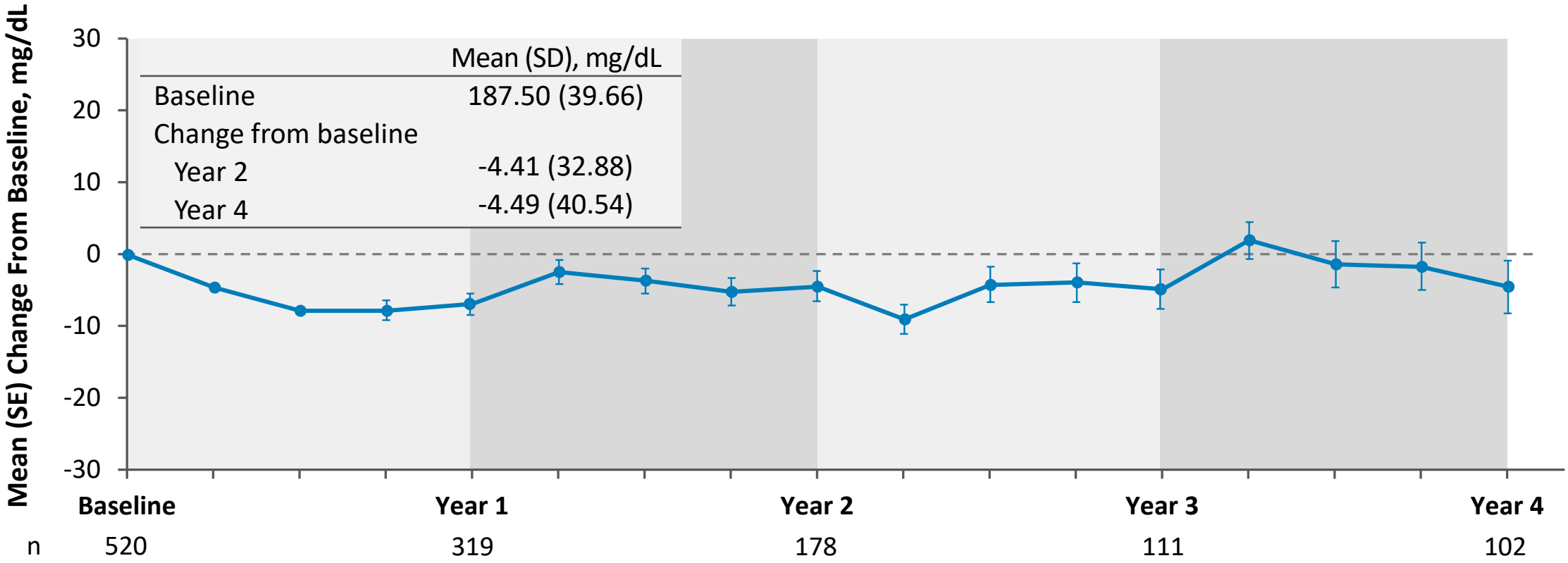
# Mean Change From Baseline in Body Weight



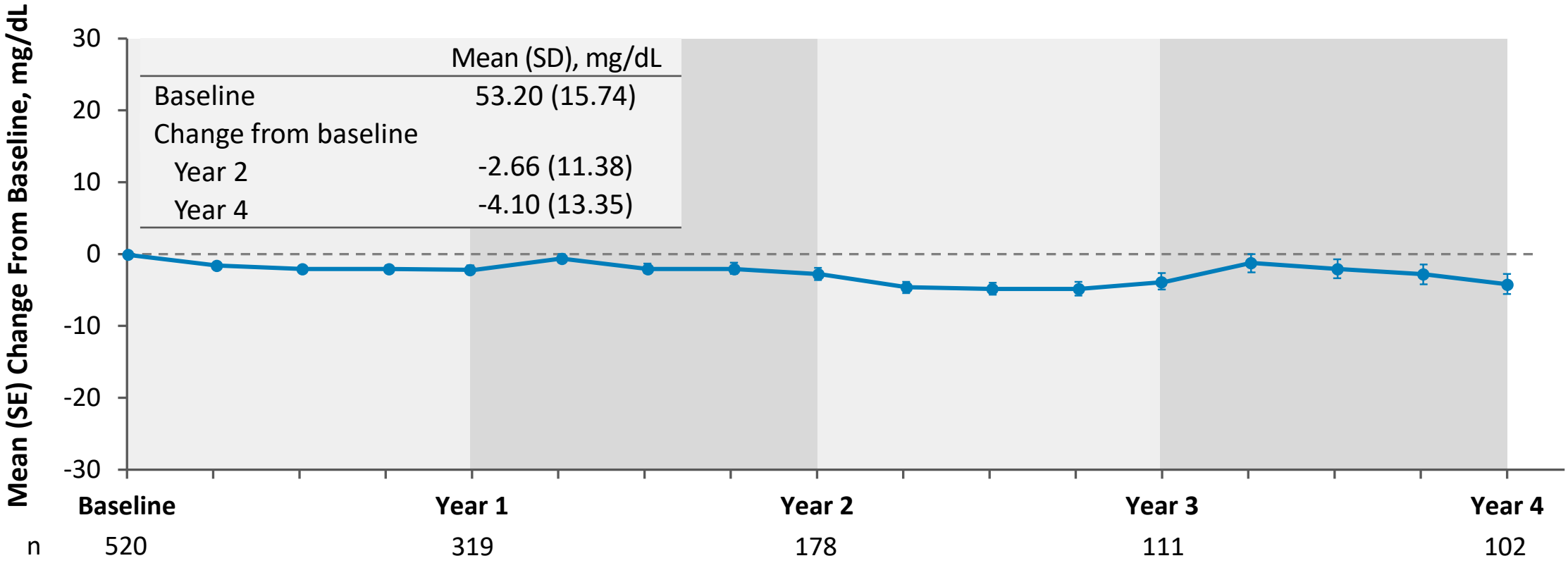
# Mean Change From Baseline in Waist Circumference



# Mean Change From Baseline in Total Cholesterol

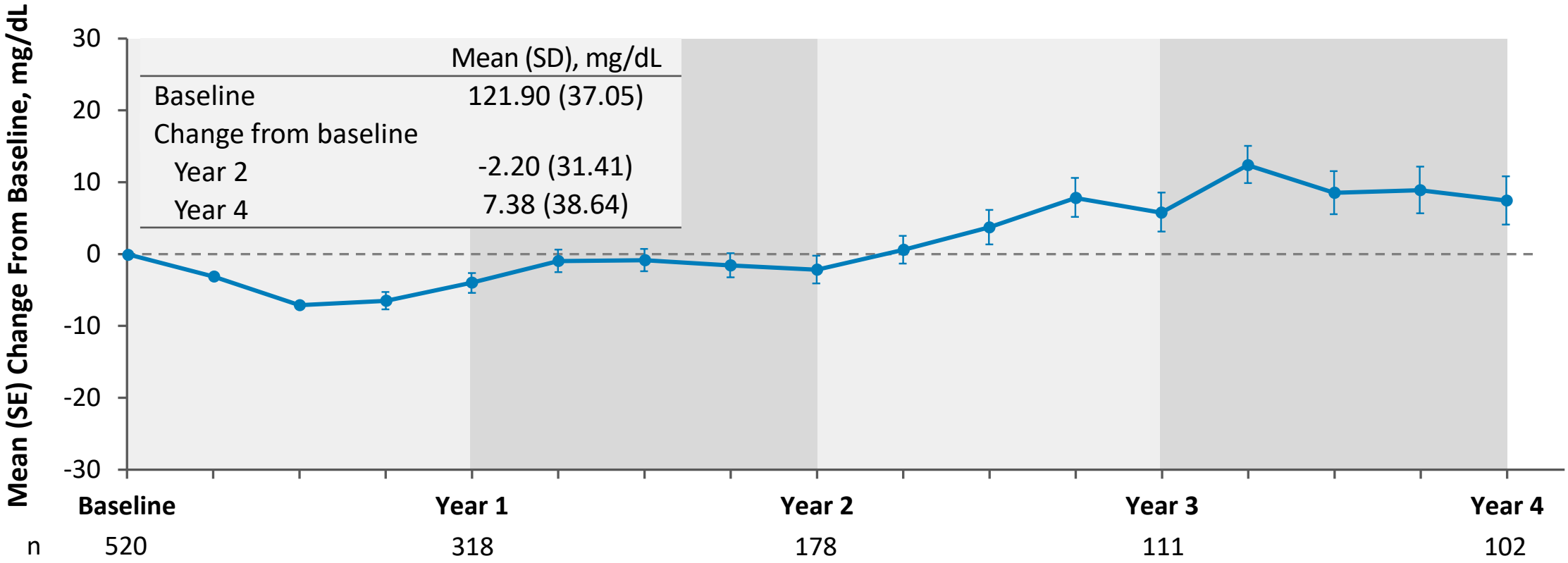


# Mean Change From Baseline in HDL Cholesterol



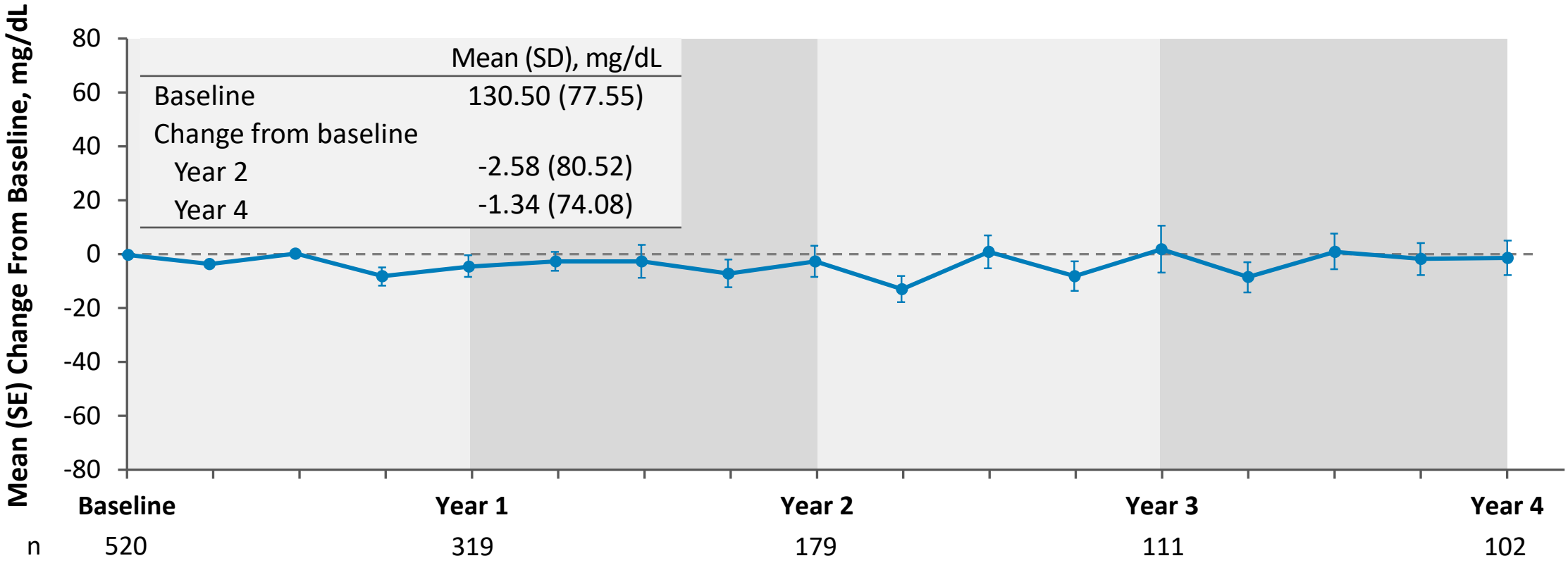

HDL, high-density lipoprotein.

# Mean Change From Baseline in LDL Cholesterol

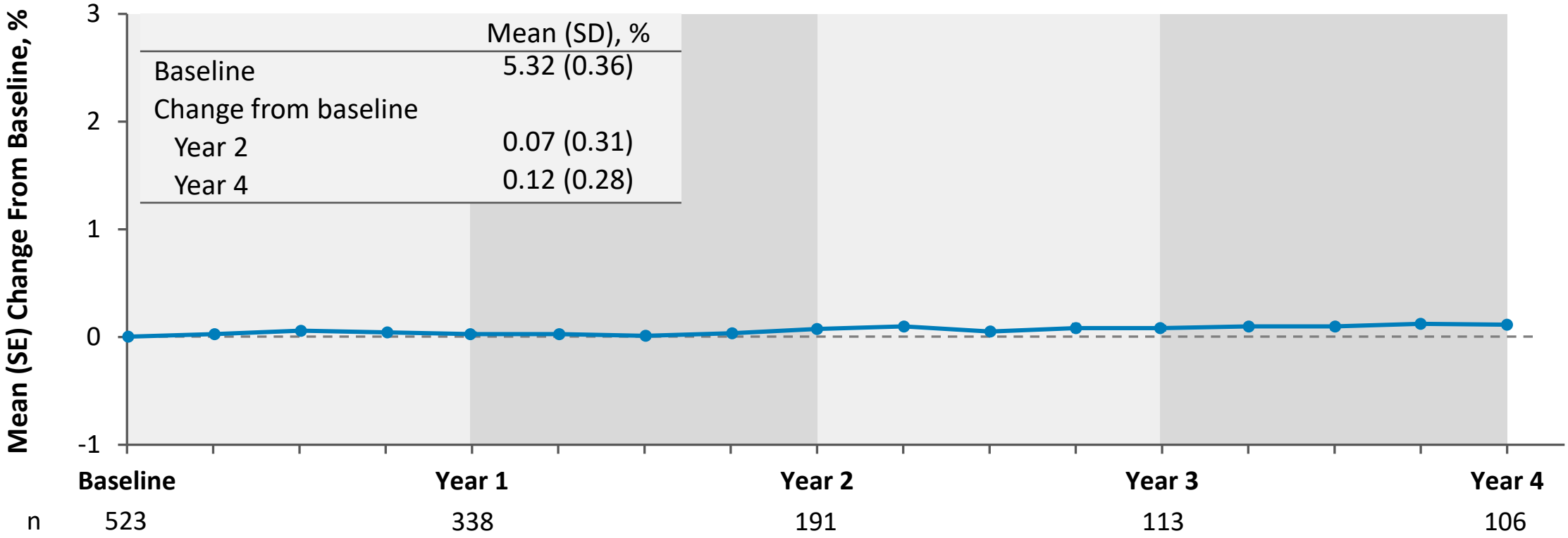



LDL, low-density lipoprotein.

# Mean Change From Baseline in Triglycerides

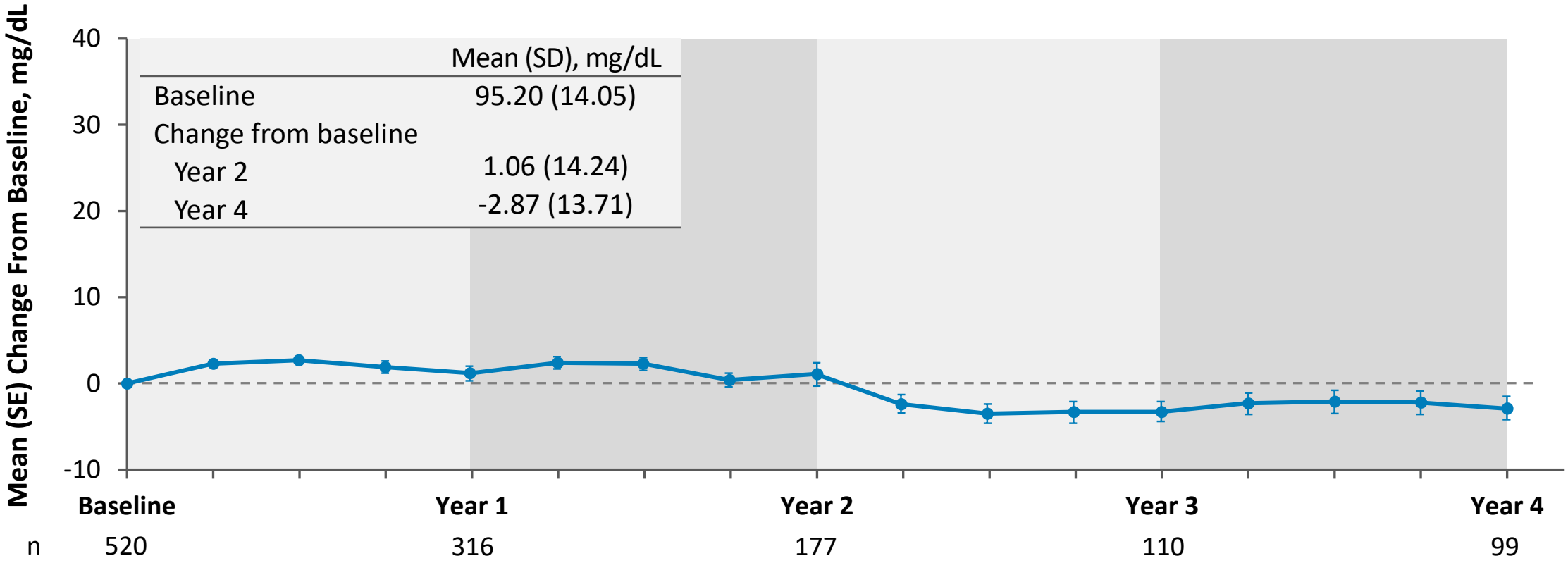


# Mean Change From Baseline in $HbA_{1c}$




$HbA_{1c}$, glycosylated hemoglobin.

# Mean Change From Baseline in Glucose



# Common Adverse Events

| Category | Patients, n (%) (N=523) |
|---|---|
| Any AE | 314 (60.0) |
| AEs by severity | |
| Mild | 143 (27.3) |
| Moderate | 148 (28.3) |
| Severe | 23 (4.4) |
| AEs leading to treatment discontinuation | 44 (8.4) |
| Any SAE | 35 (6.7) |
| SAE leading to death | 1 (0.2) |

| Category | Patients, n (%) (N=523) |
|---|---|
| Most common AEs (≥5%) | |
| Weight increase | 51 (9.8) |
| Headache | 37 (7.1) |
| Anxiety | 32 (6.1) |
| Insomnia | 31 (5.9) |
| Somnolence | 31 (5.9) |
| Nausea | 30 (5.7) |
| Weight decrease | 30 (5.7) |

AE, adverse event; SAE, serious adverse event.

# Conclusions

- In this open-label extension study, 53.7% (242/451) of eligible patients received ≥2 years of treatment, and 32.5% (109/335) received 4 years of treatment
- OLZ/SAM maintained symptom control and had a long-term safety profile over 4 years that was consistent with past observations of OLZ/SAM use[1-5] in patients with schizophrenia or bipolar I disorder
  - Small changes in body weight
  - Minimal changes in waist circumference
  - Minimal changes in metabolic parameters
- These results highlight the long-term safety and clinical benefits of OLZ/SAM for the maintenance treatment of schizophrenia and bipolar I disorder

OLZ/SAM, olanzapine combined with samidorphan.

**1.** Potkin SG, et al. *J Clin Psychiatry.* 2020;81(2):19m12769. **2.** Yagoda S, et al. *CNS Spectr*. 2021;26(4):383-392. **3.** Correll CU, et al. *Am J Psychiatry*. 2020;177(12):1168-1178. **4.** Kahn RS, et al. *Schizophr Res*. 2021;232:45-53. **5.** Kahn RS, et al. *J Clin Psychiatry*. 2023;84(3):22m14674.

# We thank our study sites and patients for participating in this study