

# ASCENT-03: Real-World External Control Arm Analysis of First-Line Sacituzumab Govitecan vs Treatment of Physician’s Choice in Patients With Metastatic Triple-Negative Breast Cancer

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## Conclusions

- In the ASCENT-03 study of first-line (1L) sacituzumab govitecan (SG) vs chemotherapy in participants with metastatic triple-negative breast cancer (mTNBC) who are not candidates for programmed death (ligand) 1 (PD-[L]1) inhibitors, post-progression crossover treatment was provided; OS data are immature
- A real-world historical chemotherapy external control arm (ECA) analysis was conducted to evaluate the impact of treatment crossover on OS with 1L SG in mTNBC from the ASCENT-03 study
- Median progression-free survival (PFS) from the weighted ECA was consistent with the ASCENT-03 chemotherapy group (6.4 vs 6.9 months), supporting the validity of using real-world data for this ECA analysis
- The SG group from ASCENT-03 demonstrated significantly improved OS vs the weighted historical chemotherapy ECA in 1L treatment of mTNBC (hazard ratio [HR], 0.56 [95% CI, 0.42-0.75];  $P < .001$ )
- Results of this exploratory ECA analysis suggest an OS benefit with 1L SG vs chemotherapy in the absence of crossover treatment in patients with mTNBC who are not candidates for PD-(L)1 inhibitors

## Plain Language Summary

- Researchers studied a medicine called sacituzumab govitecan (SG) in people with a hard-to-treat type of breast cancer called metastatic triple-negative breast cancer (mTNBC)
- In the ASCENT-03 study, participants who received SG lived longer without their cancer getting worse or dying than participants who received chemotherapy
- Some people in the ASCENT-03 study switched from chemotherapy to SG when their cancer got worse. This may make it difficult to clearly understand how each treatment affects how long participants live overall after starting the study treatment
- In the current exploratory analysis, researchers compared the results from people who received SG in ASCENT-03 with those who received standard chemotherapy (before SG was approved) but were not involved in the study and did not receive SG
- The time that people lived without their cancer getting worse was similar in the real-world chemotherapy group and the ASCENT-03 chemotherapy group; this supports the use of real-world data for this analysis
- The results showed that people who received SG lived longer than those who received chemotherapy
- Overall, the results suggest that people with mTNBC may live longer if they receive SG as their first treatment

**References:** 1. Cortés J, et al. *N Engl J Med*. 2025;393(19):1912-25. 2. Dasgupta A, et al. *Health Econ Outcomes Res*. 2026;13(2):1-7. 3. Farah E, et al. *Cancer Med*. 2024;13(13):e7447.

**Acknowledgments:** We extend our thanks to the patients, their families, and all participating investigators. This study was funded by Gilead Sciences, Inc. Writing/editorial support was provided by Sonal S Joshi, PhD, of Parexel, and funded by Gilead Sciences, Inc.

**Disclosures:** ACG-C reports consulting/advisory roles with AstraZeneca, BioNTech, Bristol Myers Squibb, Daiichi Sankyo, Gilead Sciences, Merck, Novartis, Pfizer, and TD Cowen; invited speaker roles with AstraZeneca, Bicycle Therapeutics, Bristol Myers Squibb, Daiichi Sankyo, Gilead Sciences, Merck, and Roche/Genentech; research funding to the institution from 4D Path, AstraZeneca, Bicycle Therapeutics, BioNTech, Biovicia, Bristol Myers Squibb, Case45, Daiichi Sankyo, Foundation Medicine, Gilead Sciences, Merck, Novartis, Precede Biosciences, Reveal Genomics, and Zenith Epigenetics; travel support from AstraZeneca, Daiichi Sankyo, Gilead Sciences, Merck, Novartis, Pfizer, Roche/Genentech, and Stemline Therapeutics; and steering committee participation with AstraZeneca, Daiichi Sankyo, and Merck.

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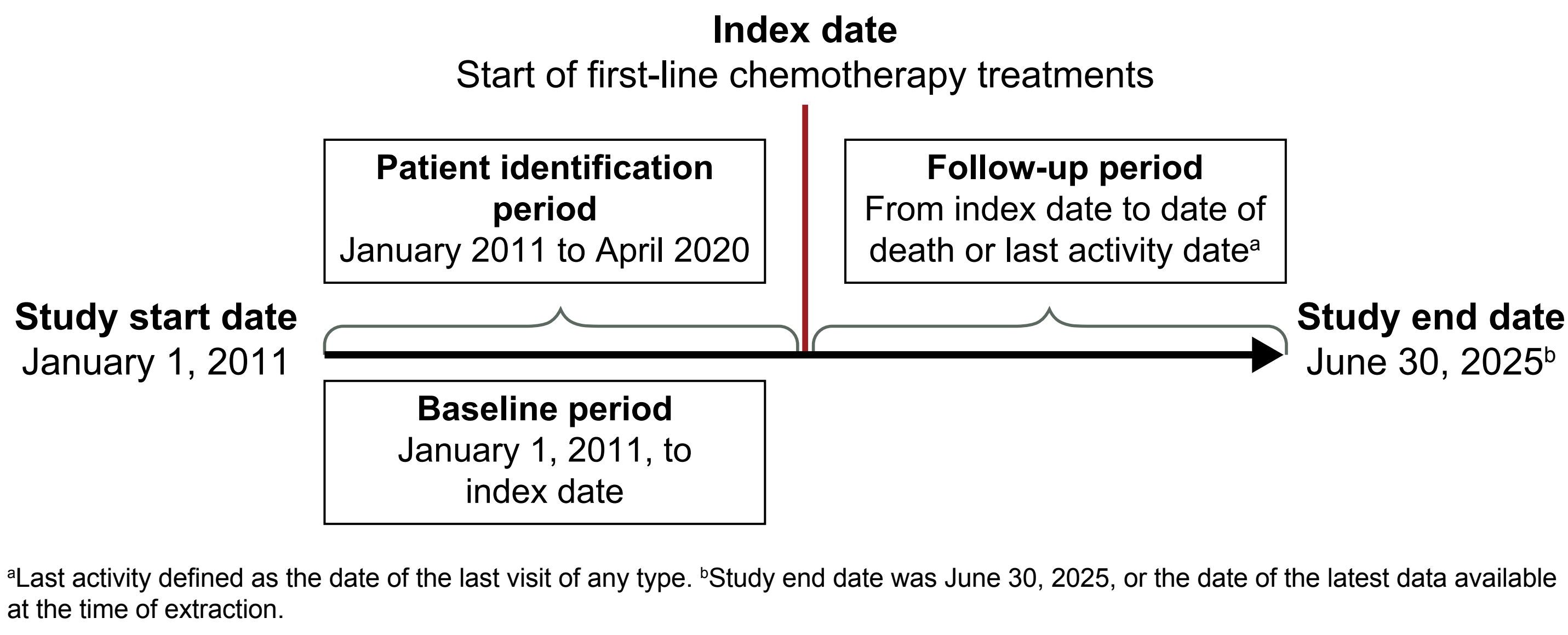
## Introduction

- In the phase 3 ASCENT-03 study (NCT05382299), 1L SG demonstrated statistically significant and clinically meaningful improvement in PFS vs chemotherapy (stratified HR, 0.62 [95% CI, 0.50-0.77];  $P < .001$ ) in participants with mTNBC who are not candidates for a PD-(L)1 inhibitor<sup>1</sup>
- SG was provided on-study as crossover to participants in the chemotherapy group following progressive disease and may also have been received commercially<sup>1</sup>
- OS data from ASCENT-03 are immature (maturity rate, 37%) and may be confounded by post-progression crossover, which can attenuate differences observed in OS<sup>1, 2</sup>
  - Median OS was 21.5 months with SG vs 20.2 months with chemotherapy; 82% of the participants who initiated subsequent treatment after chemotherapy received SG
- A real-world historical ECA can be used as a comparator to assess the efficacy of 1L treatments in a setting unaffected by crossover<sup>3</sup>
- This exploratory ECA analysis was used to evaluate the impact of treatment crossover on OS with 1L SG in mTNBC

## Methods

- The ECA was constructed using a custom-curated dataset of patients with mTNBC from the Flatiron Health Research Database who initiated 1L chemotherapy with a regimen included in the control group of the ASCENT-03 study (paclitaxel, nab-paclitaxel, or gemcitabine + carboplatin) prior to SG FDA approval (April 2020) (**Figure 1**)
- The cohort was further streamlined to select the trial-like population by utilizing key inclusion/exclusion criteria from ASCENT-03, including Eastern Cooperative Oncology Group performance status scores, adequate hematologic counts and hepatic function, and creatinine clearance
- Standardized mortality ratio (SMR) weighting was used to balance prognostic factors in the ECA to match the distribution of key prognostic factors in the ASCENT-03 study. Variables selected for matching were
  - Sex (categorical)
  - Age at index (continuous)
  - Time from initial diagnosis to metastatic diagnosis (continuous)
  - De novo metastatic disease (binary)
  - Brain, liver, lung, and bone metastasis (binary)
- Weighted Kaplan-Meier time-to-event survival analyses and weighted Cox proportional hazards models were used to evaluate survival outcomes

**Figure 1. Study Design**



## Results

- A total of 210 patients with mTNBC who initiated 1L chemotherapy between January 2011-April 2020 and met the eligibility criteria for ASCENT-03 were included in the final ECA; median follow-up was 13 months
- Fifteen (7%) patients received SG in the second-line or later
- Baseline characteristics were generally similar between the SG group from ASCENT-03 and the ECA, except for race, geographic region, and chemotherapy received (**Table 1**); the number of patients who received gemcitabine + carboplatin was higher in the ASCENT-03 chemotherapy group (44%) compared with the historical chemotherapy ECA (32%)
- Common metastatic sites in the ECA at the index date included lymph node (49%), lung (44%), bone (43%), liver (28%), and brain (11%)

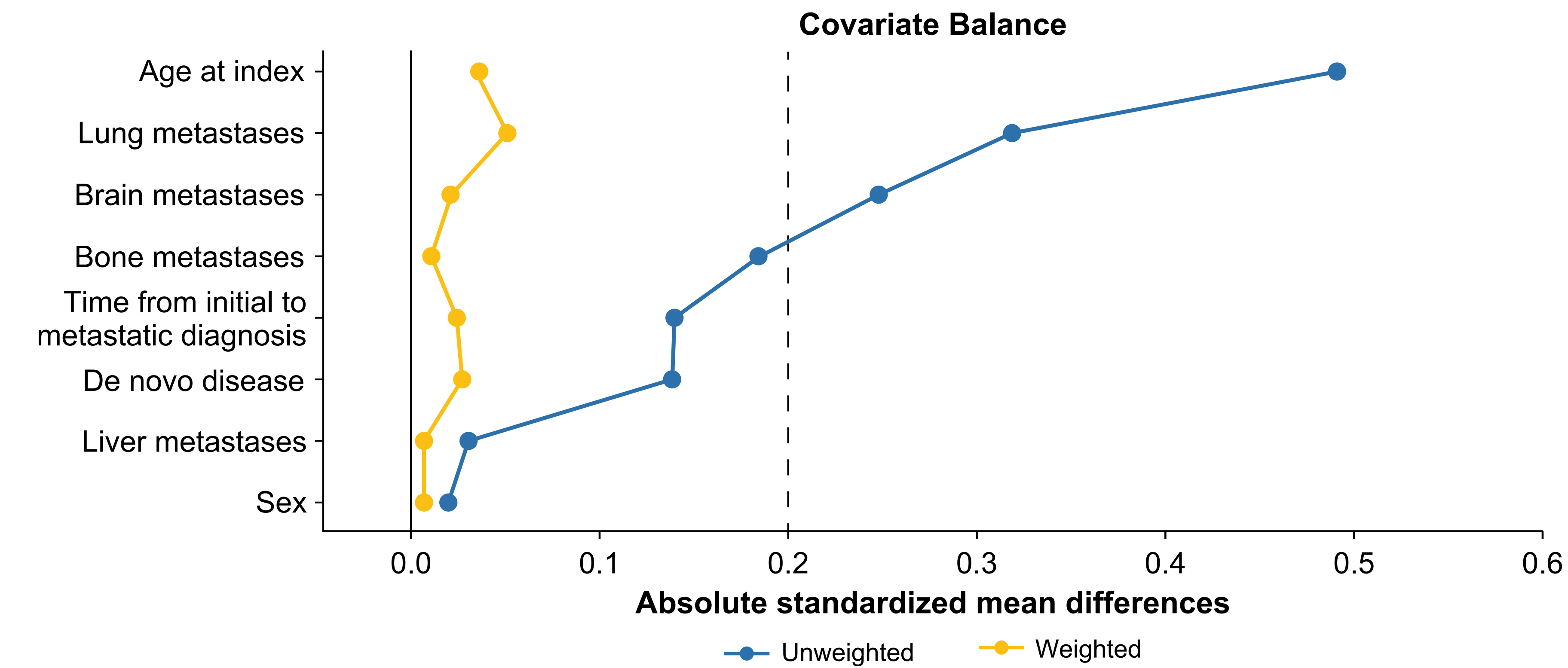
## Results

**Table 1. Demographics and Baseline Disease Characteristics**

|                                                                              | ASCENT-03 SG<br>(n = 279) | ASCENT-03 Chemotherapy<br>(n = 279) | ECA Historical Chemotherapy<br>(n = 210) |
|------------------------------------------------------------------------------|---------------------------|-------------------------------------|------------------------------------------|
| Female sex, n (%)                                                            | 278 (> 99)                | 277 (> 99)                          | 209 (> 99)                               |
| Median age, (range), years                                                   | 56 (28-84)                | 54 (23-86)                          | 62 (30-85)                               |
| Race or ethnic group, n (%)                                                  |                           |                                     |                                          |
| White                                                                        | 178 (64)                  | 178 (64)                            | 115 (55)                                 |
| Asian                                                                        | 66 (24)                   | 65 (23)                             | 6 (3)                                    |
| Black                                                                        | 10 (4)                    | 7 (3)                               | 50 (24)                                  |
| Other/not specified                                                          | 25 (9)                    | 26 (10)                             | 39 (19)                                  |
| Geographic region, n (%)                                                     |                           |                                     |                                          |
| United States/Canada/Western Europe                                          | 89 (32)                   | 89 (32)                             | 210 (100)                                |
| Rest of the world                                                            | 190 (68)                  | 190 (68)                            | —                                        |
| Metastatic sites, n (%)                                                      |                           |                                     |                                          |
| Lymph node                                                                   | 179 (64)                  | 180 (65)                            | 103 (49)                                 |
| Lung                                                                         | 166 (59)                  | 170 (61)                            | 92 (44)                                  |
| Bone                                                                         | 95 (34)                   | 87 (31)                             | 90 (43)                                  |
| Liver                                                                        | 81 (29)                   | 72 (26)                             | 58 (28)                                  |
| Brain                                                                        | 15 (5)                    | 14 (5)                              | 23 (11)                                  |
| Other                                                                        | 98 (35)                   | 84 (30)                             | 57 (27)                                  |
| ECOG PS at baseline,* n (%)                                                  |                           |                                     |                                          |
| 0                                                                            | 183 (66)                  | 187 (67)                            | 87 (41)                                  |
| 1                                                                            | 96 (34)                   | 92 (33)                             | 71 (34)                                  |
| Disease status, n (%)                                                        |                           |                                     |                                          |
| De novo                                                                      | 87 (31)                   | 88 (32)                             | 75 (36)                                  |
| Disease-free interval 6-12 months                                            | 58 (21)                   | 57 (20)                             | NA <sup>b</sup>                          |
| Disease-free interval > 12 months                                            | 134 (48)                  | 134 (48)                            |                                          |
| Time from initial to metastatic diagnosis, <sup>c</sup> median (IQR), months | 33.0 (21.9-59.2)          | 31.1 (21.6-52.4)                    | 30.6 (18.9-70.8)                         |
| Chemotherapy received                                                        |                           |                                     |                                          |
| Gemcitabine/carboplatin                                                      | 0 (0)                     | 122 (44)                            | 68 (32)                                  |
| Taxanes                                                                      | 0 (0)                     | 154 (55)                            | 142 (68)                                 |
| Follow-up duration, median (IQR), months                                     | 13.2 (9.9-17.5)           | 13.1 (9.7-17.1)                     | 13.0 (7.5-23.5)                          |

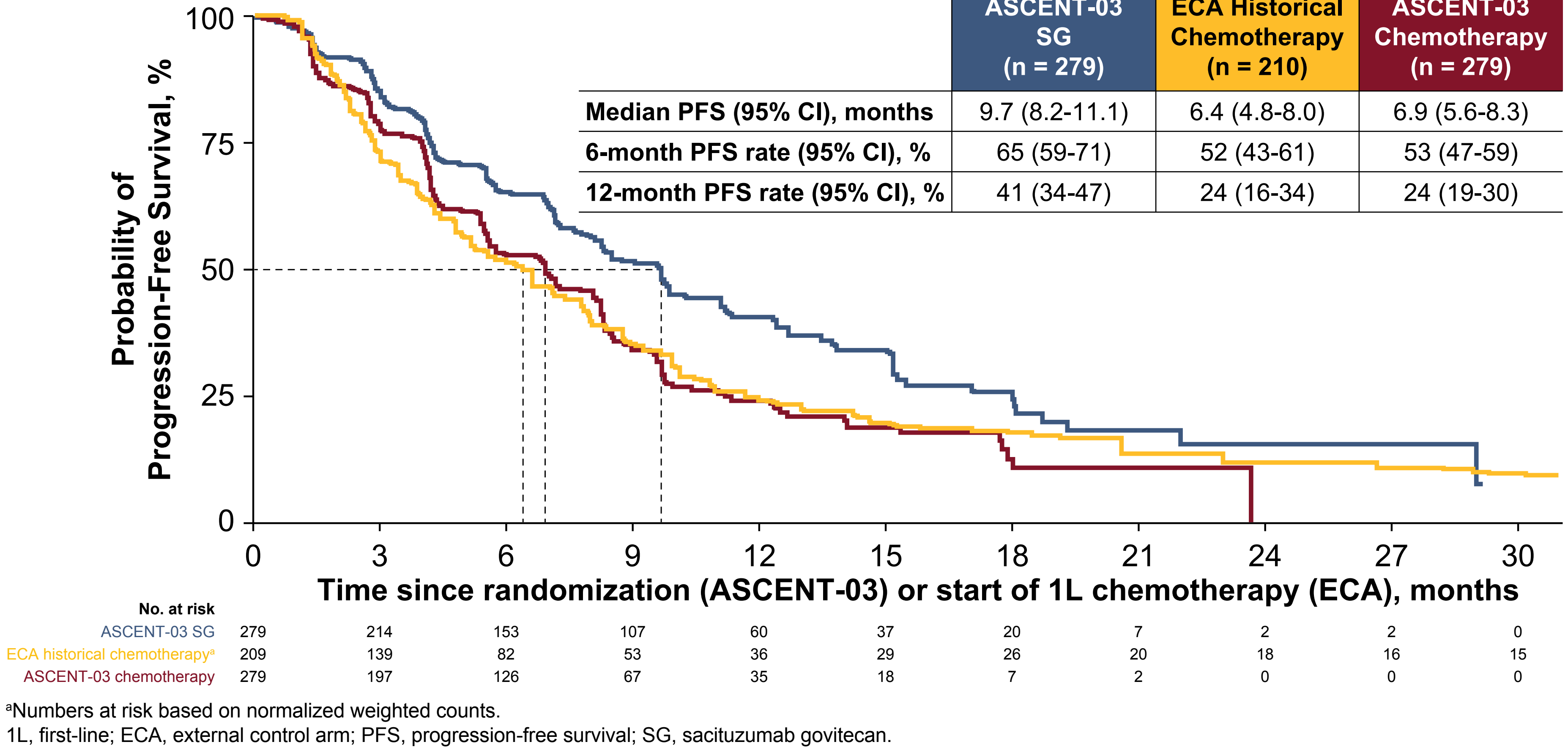
\*ECOG PS was unknown in 52 patients in the historical ECA. <sup>b</sup>Information for disease-free interval was not available in the historical ECA. <sup>c</sup>Recurrent disease only. ECA, external control arm; ECOG PS, Eastern Cooperative Oncology Group performance status; IQR, interquartile range; NA, not applicable; SG, sacituzumab govitecan.

**Figure 2. Propensity Score Matching**



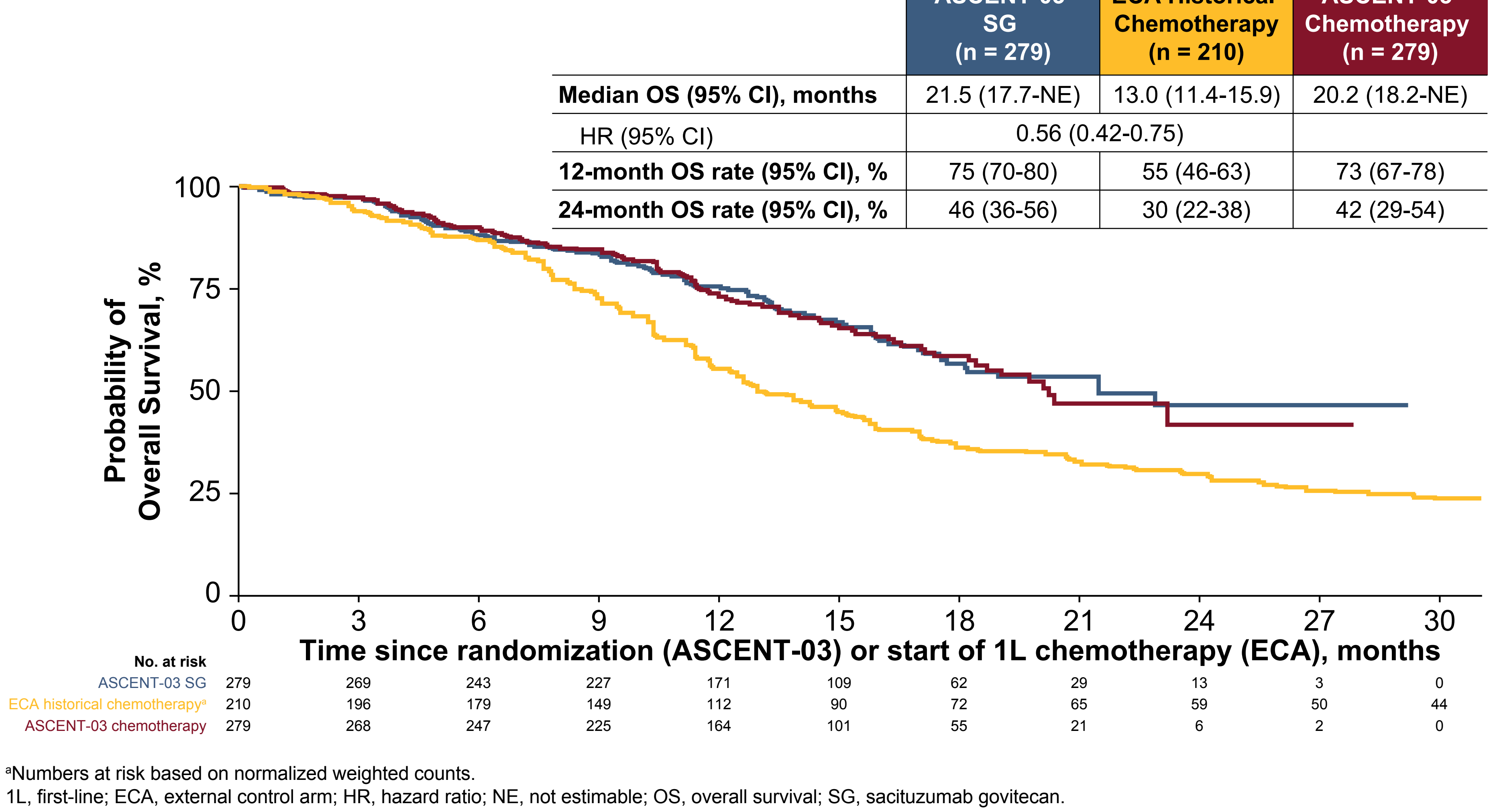
- Standardized mean differences between key prognostic factors were reduced after the historical chemotherapy ECA was weighted using SMR (**Figure 2**)

**Figure 3. Progression-Free Survival**



- After applying SMR weighting, median PFS from the historical chemotherapy ECA was consistent with the ASCENT-03 chemotherapy group (6.4 vs 6.9 months) (**Figure 3**)
- Comparison of the ASCENT-03 SG group with the weighted ECA demonstrated a significant improvement in PFS for SG vs chemotherapy, with an HR of 0.70 (95% CI, 0.53-0.92)

**Figure 4. Overall Survival**



- Median OS was significantly longer with SG from ASCENT-03 compared with chemotherapy from the weighted ECA (HR, 0.56 [95% CI, 0.42-0.75];  $P < .001$ ) (**Figure 4**)
- Following exclusion of the 15 patients in the ECA who received SG in the second-line or later, median OS was 21.5 vs 12.7 months; HR for OS decreased to 0.51 (95% CI, 0.38-0.68;  $P < .001$ )

## Limitations

- This is an exploratory analysis that curated a historical cohort to minimize the proportion of patient crossover to SG in subsequent lines, and, as such, it does not represent the current treatment landscape and outcomes with contemporary therapies
- OS in the ECA cohort in this analysis was slightly lower than that observed in chemotherapy arms in similar clinical trials; however, this was expected given differences between real-world practice and controlled trial settings
- PD-L1 status and disease-free interval were not captured in the historical dataset and therefore could not be evaluated