Adjuvant Atezolizumab for Early Triple-Negative Breast Cancer

The ALEXANDRA/IMpassion030 Randomized Clinical Trial

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Key Points

Question Does the addition of 1 year of immune therapy to standard-of-care post-operative chemotherapy reduce the risk of recurrence in patients with high-risk early-stage triple-negative breast cancer (TNBC) after surgery?

Findings This international, open-label, phase 3 trial randomized 2199 patients with stage II/III TNBC who had completed definitive surgery to receive standard-of-care curative-intent chemotherapy with or without atezolizumab-mediated immune therapy and did not demonstrate an improvement in recurrence rates and/or death with the addition of immune therapy (primary end point: invasive disease-free survival).

Meaning The addition of the immunotherapy drug atezolizumab to postoperative chemotherapy is not effective in patients with breast cancer of the TNBC subtype who are at high risk of developing metastases.

IMPORTANCE Triple-negative breast cancer (TNBC) is an aggressive subtype with a high incidence in young patients, a high incidence in Non-Hispanic black women, and a high risk of progression to metastatic cancer, a devastating sequela with a 12- to 18-month life expectancy. Until recently, one strategy for treating early-stage TNBC was chemotherapy after surgery. However, it was not known whether the addition of immune therapy to post-surgery chemotherapy would be beneficial.

OBJECTIVE To evaluate the addition of immune therapy in the form of atezolizumab to postoperative chemotherapy in patients with the high-risk TNBC subtype.

DESIGN, SETTING, AND PARTICIPANTS In this open-label international randomized phase 3 trial conducted in more than 330 centers in 31 countries, patients undergoing surgery as initial treatment for stage II/III triple-negative breast cancer were enrolled between August 2, 2018, and November 11, 2022. The last patient follow-up was on August 18, 2023.

INTERVENTIONS Patients were randomized (1:1) to receive standard chemotherapy for 20 weeks with or without the immune therapy drug atezolizumab for up to 1 year.

MAIN OUTCOMES AND MEASURES The primary end point was invasive disease-free survival (time between randomization and invasive breast cancer in the same or opposite breast, recurrence elsewhere in the body, or death from any cause).

RESULTS The median age of enrolled patients was 53 years and most self-reported as being of White or Asian race and neither Latino nor Hispanic ethnicity. The study independent data monitoring committee halted enrollment at 2199 of 2300 planned patients. All patients stopped atezolizumab following a planned early interim and futility analysis. The trial continued to a premature final analysis. With invasive disease-free survival events in 141 (12.8%) patients treated with atezolizumab–chemotherapy and 125 (11.4%) with chemotherapy alone (median follow-up 32 months), the final stratified invasive disease-free

survival hazard ratio was 1.11 (95% CI, 0.87–1.42; *P* = .38). Compared with chemotherapy alone, atezolizumab–chemotherapy was associated with more treatment-related grade 3/4 adverse events (54% vs 44%) but similar incidences of fatal adverse events (0.8% vs 0.6%) and adverse events leading to chemotherapy discontinuation. Chemotherapy exposure was similar in the 2 treatment groups.

CONCLUSIONS AND RELEVANCE The addition of the immune therapy drug atezolizumab to chemotherapy after surgery did not provide benefit among patients with the TNBC subtype who are at high risk of recurrent disease.

TRIAL REGISTRATION ClinicalTrials.gov identifier: NCT03498716 (https://clinicaltrials.gov/study/NCT03498716)

“Triple-negative” breast cancer (TNBC) is a breast cancer subtype defined by the absence of *ERBB2*/HER2 DNA amplification/protein overexpression and low/no expression of estrogen and progesterone receptors. TNBC is associated with a high risk of progression to metastatic disease, [1] higher incidence in younger women compared to other subtypes, [2-4] and higher incidence in Non-Hispanic black women. [5,6] Historically, approximately one-third of individuals with stage II–III TNBC experience a metastatic recurrence despite best-available chemotherapy within 2–3 years after an early-stage diagnosis, which, in turn, has a life expectancy of only 12–18 months. [1] Consequently, innovation beyond conventional chemotherapy has been an unmet need. This trial investigated whether the efficacy of curative-intent adjuvant chemotherapy for TNBC is improved by adding immune therapy, which has become a standard in many other solid tumors and for selected patients with advanced TNBC. The introduction of modern immune therapy (blocking either the immunomodulatory receptor CTLA-4 or the immunoinhibitory receptor programmed cell death protein [PD]-1 and its ligand programmed death-ligand 1 [PD-L1]) has revolutionized clinical oncology. [7] Pivotal trials evaluating the addition of immune checkpoint inhibition to conventional chemotherapy demonstrated improved outcomes in several solid tumor types characterized by high tumor mutational burden, [8] including melanoma, [9-12] non-small-cell lung, [13,14] and urothelial[15] cancers. Breast cancer, which has intermediate tumor mutational burden, was thus a logical target and early clinical data of immunotherapy with chemotherapy in metastatic TNBC were encouraging. [16-19] Evaluation of atezolizumab for early-stage TNBC was subsequently supported by phase III results demonstrating significantly improved outcomes with the addition of immunotherapy to first-line chemotherapy for biomarker-selected (tumors with high expression of the target, PD-L1) advanced TNBC. [20-23]

The ALEXANDRA/IMpassion030 trial investigated combining atezolizumab with standard adjuvant chemotherapy for patients who underwent surgery as their first treatment for stage II–III TNBC. We report results from the final analysis.

Methods

ALEXANDRA/IMpassion030 (NCT03498716) was an international, open-label, randomized phase 3 trial evaluating atezolizumab combined with standard adjuvant chemotherapy and continued as maintenance for early-stage TNBC. The trial protocol, amendments, informed consent forms, and patient information were approved by each site's ethics committee before study initiation. All patients provided written informed consent before enrollment. None received a stipend for participation. All authors attest that the trial was conducted in accordance with the protocol, its amendments, and Good Clinical Practice standards.

Patients

Eligible patients were aged ≥18 years with non-metastatic operable stage II–III TNBC (no *ERBB2* amplification/HER2 overexpression, <1% expression of estrogen and progesterone receptors, determined at a central laboratory according to American Society of Clinical Oncology/College of American Pathologists criteria[24-26]) that had been adequately excised (breast-conserving surgery or mastectomy). Sentinel lymph node biopsy and/or axillary lymph node dissection was mandatory to evaluate pathologic nodal status. It was planned to enroll a population enriched (≥50%) for node-positive disease; patients with node-negative disease had to have a pathologic tumor size >2 cm. A representative formalin-fixed paraffin-embedded tumor specimen was required from all patients before enrollment for central evaluation of PD-L1 status using the VENTANA SP142 immunohistochemistry assay. Patients with a history of invasive breast cancer, any T4 tumor, prior systemic anticancer treatment for the currently diagnosed breast cancer, or prior anthracycline, taxane, or immune checkpoint inhibitor therapy were ineligible. The protocol details complete eligibility criteria (available in Supplement 1).

Treatment

All patients received standard combination chemotherapy comprising weekly paclitaxel 80 mg/m^2 for 12 weeks followed by dose-dense doxorubicin 60 mg/m^2 or epirubicin 90 mg/m^2 (investigator's choice) given with cyclophosphamide 600 mg/m^2 every 2 weeks for 4 cycles, supported with granulocyte(-macrophage) colony-stimulating factor. Patients were randomized in a 1:1 ratio to receive chemotherapy with or without atezolizumab 840 mg every 2 weeks for up to 10 doses, followed in the experimental group by maintenance atezolizumab 1200 mg every 3 weeks up to 1 year in total. Randomization used permuted blocks, with fixed block size and the following stratification factors: axillary nodal status (0 vs 1–3 vs ≥4 positive lymph nodes); surgical approach (breast conserving vs mastectomy); and tumor PD-L1 status (IC0 [PD-L1 immune cells (ICs) <1%] vs IC1–3 [PD-L1 IC ≥1%]). The random allocations were generated by an external IXRS company, with participants enrolled by each site using the IXRS. In this open-label trial, the study team was blinded to PD-L1 status and had restricted access to the randomization lists.

End Points

The primary end point was invasive disease-free survival (iDFS), defined as the interval between randomization and first ipsilateral invasive breast tumor recurrence, ipsilateral local-regional invasive breast cancer recurrence, ipsilateral second primary invasive breast cancer, contralateral invasive breast cancer, distant recurrence, or death from any cause in the intent-to-treat (ITT) population. Secondary end points included iDFS in the populations with PD-L1-positive (IC ≥1%) TNBC and node-positive TNBC, overall survival, iDFS including second primary non-breast invasive cancer, recurrence-free interval, distant

recurrence-free interval, disease-free survival, and safety (occurrence and severity of adverse events [AEs]).

Statistical Analysis

It was planned to enroll 2300 patients from 31 countries. Early versions of the statistical analysis plan included 1 planned interim analysis at 80% information (310 of 388 iDFS events). The sample size for the analysis of iDFS was determined using Cytel East 6, reproduced (and updated for changes to the number of interim analyses) in R package rpact, [27-29] assuming approximately 80% power to detect an assumed hazard ratio of 0.75 using a 2-sided stratified log-rank test at the 0.05 significance level (type I error rate), piecewise annual hazard rates (0.047, 0.108, 0.035, 0.038, 0.029, 0.029, 0.014) for the control arm based on previous adjuvant TNBC trials, [30-32] 2.5% annual loss to follow-up, one interim analysis, and accrual over 51 months.

In November 2022, after enrolling 2199 (96%) of the planned patients, the independent data monitoring committee recommended temporarily halting recruitment, resulting in a Health Authority request to advance the planned interim analysis to mid-March 2023 and add a futility assessment. The study protocol (Supplement 1) and statistical analysis plan (Supplement 2) were updated to include an additional interim analysis at approximately 62% information (242 iDFS events) with a non-binding futility analysis (futility boundary: hazard ratio >1). The second interim analysis at 80% information and the final analysis were updated to occur after 312 and 390 iDFS events, respectively. Other assumptions were unchanged. The final analysis of the key secondary end points including overall survival was planned according to the fixed-sequence hierarchical testing procedure. [33,34]

On March 15, 2023, following the interim and futility analyses and based on the independent data monitoring committee's recommendations, atezolizumab treatment was stopped and enrollment to the ALEXANDRA/IMpassion030 trial was permanently discontinued. By the final database lock (November 20, 2023), 266 of the planned 390 iDFS events had occurred. The final significance boundary for iDFS was calculated as 0.04988 (2-sided), considering the interim and final analyses at 239 and 266 iDFS events, respectively, and the overall protocol-specified significance level of 0.05 (type I error rate). Boundaries for statistical significance were determined based on the Lan-DeMets alpha spending function with an O'Brien-Fleming boundary[35] with fixed-sequence hierarchical group-sequential testing, strongly protecting the family-wise error rate. Key secondary end points were to be tested only if the primary end point and preceding secondary end points crossed the significance boundaries.

Efficacy was analyzed in the ITT population, comprising all patients as randomized. Safety was analyzed in the safety population, comprising all patients who received at least 1 dose of study medication, as treated.

Assessments

Race (and ethnicity in patients enrolled in the USA) was self-reported by patients from a fixed list according to each country's regulations to provide a more comprehensive description of the study population. Disease status was evaluated at clinic visits every 3 months during study treatment and for up to 3 years after randomization; every 6 months from 3 to 5 years after randomization; and annually thereafter until the study end. AEs were graded using National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0 and patients were followed until 30 days after the last study dose. Importantly, this resulted in longer follow-up in the atezolizumab group (until 30 days after the last dose of maintenance atezolizumab at 1 year) than in the control group (until 30 days after the last

anthracycline/cyclophosphamide dose at 19 weeks). Additionally, during the maintenance phase, clinic visits were every 3 weeks in the atezolizumab group vs every 6 weeks in the chemotherapy-alone group.

Trial Oversight

The trial was sponsored by F. Hoffmann-La Roche Ltd and conducted in collaboration with the Breast International Group (BIG), Brussels, Belgium, with the participation of BIG member groups, Alliance Foundation Trials, and independent sites in Asia, Europe, North and South America, and Australia. Samples were tested centrally at the European Institute of Oncology and Q Squared Solutions (China). Data management was conducted by Institut Jules Bordet/Clinical Trials Support Unit, Brussels, Belgium and statistical analyses by Frontier Science Foundation, Scotland. The sponsor had no access to the full database before the steering committee released the results.

We followed the CONSORT reporting guidelines for randomized trials.

Results

Patients and Treatment

Between August 2, 2018, and November 11, 2022, 2199 patients were enrolled from >330 centers in 31 countries. Of these, 1101 were randomized to atezolizumab-chemotherapy and 1098 to chemotherapy alone; 2177 were treated (Figure 1). Overall, 49% of patients had node-positive disease, 71% had PD-L1-positive tumors, and 61% had poorly differentiated histology; the highest recruiting countries were Russian Federation (17%), Ukraine (13%), and China (12%) (Table 1 and eTable 1 in Supplement 3). The COVID-19 pandemic and

Russia-Ukraine conflict had only a minor impact on study conduct and no impact on the results and conclusions.

The median duration of atezolizumab treatment was 11.5 (interquartile range 9.4–11.8, range 0–12.7) months, corresponding to 15 (range 1–16) cycles. Among 328 patients (30%) discontinuing atezolizumab prematurely, the most common reasons were AEs (13%), patient withdrawal (5%), study termination (4%), and disease recurrence (4%). In both treatment groups, patients received a median of 4 (range 1–4) doses of cyclophosphamide, epirubicin/doxorubicin, and 12 (range 1–13) doses of paclitaxel.

Efficacy

Median follow-up at the final analysis was 32 (range 0–59) months. In the ITT population, iDFS events had been recorded in 266 patients: 141 (12.8%) in the atezolizumab–chemotherapy group and 125 (11.4%) in the chemotherapy-alone group (Figure 2A). The final stratified hazard ratio for iDFS was 1.11 (95% confidence interval [CI], 0.87–1.42; *P* = .38). eTable 2 in Supplement 3 shows sensitivity analyses. Descriptive subgroup analyses of iDFS, including PD-L1-positive TNBC, showed no benefit from atezolizumab–chemotherapy (Figure 2B and eFigure 1 in Supplement 3). Descriptive analysis of secondary efficacy end points suggested consistency with the iDFS results (Table 2 and eFigure 2 in Supplement 3).

Safety

Compared with chemotherapy alone, atezolizumab–chemotherapy was associated with more treatment-related grade 3/4 AEs (54% vs 44%) and treatment-related serious AEs (19% vs 10%) (eTable 3 in Supplement 3). Fifteen patients had fatal AEs: 9 (0.8%) treated

with atezolizumab–chemotherapy and 6 (0.6%) with chemotherapy alone (eTables 3 and 4 in Supplement 3). Only 1 of these deaths was considered by the investigator to be treatment related (paclitaxel-attributed pneumonia in a 79-year-old patient receiving chemotherapy alone). AEs led to atezolizumab discontinuation in 13% of patients treated with atezolizumab–chemotherapy (during the induction phase in 8%). However, chemotherapy discontinuation for AEs was infrequent in both groups and the addition of atezolizumab did not affect chemotherapy dose intensity (eTable 3 in Supplement 3).

Most AEs occurred at similar incidences in the 2 treatment groups (Table 3). The most common with both regimens were alopecia, nausea, anemia, and fatigue. Compared with chemotherapy alone, atezolizumab–chemotherapy was associated with higher incidences of diarrhea (26% vs 17%), increased aspartate aminotransferase (23% vs 15%), rash (16% vs 8%), and hypothyroidism (15% vs 1%). The most common immune-mediated AEs were rash, hepatitis (predominantly laboratory abnormalities emerging during the induction period), and hypothyroidism (Table 3 and eTable 5 in Supplement 3). Atezolizumab was interrupted for immune-mediated AEs in 252 patients (23%).

Discussion

ALEXANDRA/IMpassion030 is, to our knowledge, the only phase 3 randomized trial in high-risk early stage TNBC to evaluate adding a PD-(L)1 inhibitor to adjuvant chemotherapy in patients who undergo surgery as their initial treatment. In ALEXANDRA/IMpassion030, postoperative atezolizumab-mediated immune therapy did not add benefit to standard-of-care chemotherapy after surgery. The hazard ratio for iDFS of 1.11 (95% CI, 0.87–1.42) and consistent descriptive results for secondary efficacy end points do not support adding atezolizumab to adjuvant chemotherapy in patients who have undergone primary surgery for early-stage TNBC. Safety results were consistent with the known safety profile of atezolizumab in early-stage TNBC (IMpassion031[36]) and across indications. Atezolizumab

was associated with increased incidences of treatment-related grade 3/4 and serious AEs, although more frequent visits during maintenance atezolizumab bias comparison with chemotherapy alone. Atezolizumab did not compromise delivery of the standard-of-care chemotherapy backbone.

The negative results from ALEXANDRA/IMpassion030 contrast with those from randomized trials evaluating PD-(L)1 inhibitors in the neoadjuvant setting demonstrating significantly improved outcomes vs chemotherapy alone.[36-40] In the KEYNOTE-522 trial, pCR rate, event-free survival (coprimary end points) and overall survival (secondary end point) were significantly improved with pembrolizumab added to neoadjuvant chemotherapy followed by adjuvant pembrolizumab after surgery;[37,38,41] consequently, pre- and postoperative pembrolizumab therapy has become the standard of care for otherwise unselected stage II–III TNBC.[42] The smaller IMpassion031 trial also demonstrated significantly improved pCR rate (primary end point) with atezolizumab added to neoadjuvant chemotherapy and a suggestion of improved event-free, disease-free, and overall survival,[43] although the trial was neither powered nor designed to detect differences in these end points.[36] In contrast, the NeoTRIP trial did not demonstrate benefit from atezolizumab in the neoadjuvant setting, with no improvement in the primary end point of event-free survival[44] nor pCR rate,[45] although differences in trial design (e.g., lack of anthracycline) may have contributed to the different outcome.

A reasonable interpretation of the accumulating evidence might be that neoadjuvant initiation of immunotherapy is more effective than adjuvant administration alone.[46] As treatment stimulates immune cells close to the tumor, postoperative immune checkpoint inhibitor application, after removing the primary tumor and lymph nodes, may not represent the optimal biologic context for immunotherapy. Preclinical research in TNBC mouse models indicated greater efficacy of neoadjuvant vs adjuvant immunotherapy.[46] Interestingly, in patients with resectable stage III/IV melanoma, event-free survival was significantly longer

with perioperative than adjuvant-only pembrolizumab.[47] This finding appears consistent with cumulative findings in early-stage TNBC, emphasizing the importance of preoperative immune checkpoint blockade regimens in TNBC and moving away from offering adjuvant-only treatment to patients eligible for chemo-immunotherapy for stage II–III TNBC. We cannot exclude the possibility that the ALEXANDRA/IMpassion030 efficacy and safety results could have been different had another immune checkpoint inhibitor been investigated in this trial. The phase 3 trial of first-line pembrolizumab in advanced TNBC demonstrated significant improvement across end points,[22,23] whereas more heterogenous results have been seen for atezolizumab across three phase 3 trials in advanced TNBC (positive IMpassion130 trial,[20,21] negative IMpassion131[48] and IMpassion132[49] trials), albeit there are important differences in trial designs, chemotherapy backbones, patient populations, and treatment settings. The ongoing placebo-controlled GeparDouze/NSABP B-59 trial[50] with a design similar to KEYNOTE-522 will inform whether preoperative initiation of atezolizumab with chemotherapy followed by postoperative atezolizumab improves long-term outcomes.

ALEXANDRA/IMpassion030 provides the only results on cancer immunotherapy plus chemotherapy as adjuvant-only treatment and no other immunotherapy trials are being investigated in this setting. Based on ALEXANDRA/IMpassion030 results, patients who receive surgery before any chemotherapy should not receive atezolizumab with their postoperative chemotherapy. The lack of benefit from standard adjuvant atezolizumab, together with the overall survival benefit observed with perioperative pembrolizumab in the KEYNOTE-522 trial, suggest that the preferred strategy for patients with high-risk TNBC is initial chemo-immunotherapy followed by surgery.[42] Globally, many patients with stage II–III TNBC still have surgery as their initial treatment.[51,52] Therefore, it is critical that findings from ALEXANDRA/IMpassion030 are considered in multidisciplinary team discussions at the time of diagnosis.

Two trials aim to answer whether adjuvant immunotherapy offers benefit to patients with TNBC who have residual disease after neoadjuvant chemotherapy and surgery. In this post-neoadjuvant TNBC setting, recent results from the A-BRAVE trial, although negative for the primary end point of disease-free survival, [53] suggest improved overall survival (secondary end point) in patients receiving single-agent avelumab for residual disease following neoadjuvant chemotherapy. The ongoing randomized phase 3 SWOG S1418/BR-006 trial (NCT02954874) in a similar post-neoadjuvant setting is comparing 1 year of pembrolizumab vs observation in patients with residual disease after neoadjuvant chemotherapy who have received standard adjuvant therapy after surgery. It remains to be seen whether immune checkpoint blockade plays a role in this very specific high-risk setting but, in both trials, systemic chemotherapy is being given before surgery.

Important study strengths include its global footprint, the large sample size, its unique nature as the only phase 3 trial evaluating immune checkpoint blockade as pure adjuvant therapy for TNBC, and central pathology review.

Limitations

There are several limitations to this trial. First, the ALEXANDRA/IMpassion030 trial was discontinued after 266 of the required 390 iDFS events for final analysis. Having crossed the prespecified (non-binding) futility boundary for iDFS, the likelihood of demonstrating a significant improvement in iDFS was deemed too low to justify continuing the trial. The hierarchical design means that analysis of all secondary end points is only descriptive and exploratory. Second, the premature trial termination shortened follow-up, thus long-term safety information is limited and late-onset AEs may not be captured. Third, the open-label design and more frequent monitoring throughout maintenance therapy in the atezolizumab–chemotherapy group may have introduced bias. Fourth, the paclitaxel chemotherapy backbone may raise questions, given the differing outcomes in the metastatic

setting with atezolizumab combined with nab-paclitaxel in the IMpassion130 trial (clinically relevant overall survival improvement) [20,21] and paclitaxel in the IMpassion131 trial (no benefit). [48] The fifth limitation is that *BRCA* status is available for only around 20% of patients enrolled in the trial. Sixth, despite enrolling globally, <1% of patients were Black.

Conclusion

Adding the immune checkpoint inhibitor atezolizumab to postoperative chemotherapy did not reduce risk of recurrence or death for patients with high-risk early-stage TNBC.

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preparation, participated in writing or critically reviewing the manuscript, approved it for submission, and vouch for the accuracy and completeness of the data reported.

Author Contributions: A Bailey and T Perretti had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Figure legends

Figure 1. Recruitment, Randomization and Follow-up in the ALEXANDRA/IMpassion030 trial

CT, chemotherapy.

Figure 2. Final Analysis of iDFS in the ITT Population: Kaplan–Meier Plot with Hazard Ratio Estimated by Stratified Cox Regression with the Following Strata: Axillary Nodal Status, Surgery (Breast Conserving vs. Mastectomy), and Tumor PD-L1 Status. P-Value Estimated by Stratified Log-Rank Test.

Median (Q1–Q3) follow-up was 32.3 (22.3–41.3) months in the atezolizumab + CT group and 31.9 (22.5–41.2) months in the CT-alone group. The Kaplan–Meier plot is truncated at 48 months, when 165 patients (<8%) remained in follow-up.

CT, chemotherapy; iDFS, invasive disease-free survival; ITT, intent-to-treat.

Figure 3. Forest Plot Showing Final Unstratified Analysis of iDFS in Key Subgroups, with Hazard Ratios Estimated by Unstratified Cox Regression.

The dashed line represents the hazard ratio for all patients.

CT, chemotherapy; ECOG PS, Eastern Cooperative Oncology Group Performance Status; PD-L1, programmed death ligand 1.

Table 1. Baseline Characteristics[a]		
Characteristic	**Atezolizumab + Chemotherapy (n = 1101)**	**Chemotherapy Alone (n = 1098)**
Age		
Median (q1, q3), yr	53 (44–61)	53 (44–62)
<65 years	916 (83)	905 (82)
≥65 years	185 (17)	193 (18)
Self-reported race		
American Indian/Alaska Native	29/1015 (3)	28/999 (3)
Asian	423/1015 (42)	401/999 (40)
Black/African American	8/1015 (1)	2 (<0.5)
White	554/1015 (55)	567 (57)
Other[b]	1 (<0.5)	1 (<0.5)
Self-reported ethnicity		
Hispanic or Latino	75/1025 (7)	100/1006 (10)
Not Hispanic or Latino	950/1025 (93)	906/1006 (90)
Geographic region		
Asia[c]	423 (38)	395 (36)
Europe[d]	410 (37)	387 (35)
Russian Federation	179 (16)	188 (17)
South America[e]	66 (6)	93 (8)
USA	14 (1)	17 (2)
Australia	9 (1)	18 (2)
ECOG performance status		
0	887 (81)	895 (82)
1	214 (19)	203 (18)
Histology		
Ductal not otherwise specified	841 (76)	813 (74)
Lobular	39 (4)	54 (5)
Ductal with medullary features	27 (2)	52 (5)
Metaplastic	50 (5)	47 (4)
Tubular	9 (1)	14 (1)
Mucinous	3 (<0.5)	3 (<0.5)
Other	154 (14)	150 (14)
Histologic grade at screening		

Table 1. Baseline Characteristics[a]		
Characteristic	**Atezolizumab + Chemotherapy (n = 1101)**	**Chemotherapy Alone (n = 1098)**
Poorly differentiated	686/954 (72)	653/965 (68)
Moderately differentiated	205/954 (21)	234/965 (24)
Well differentiated	59/954 (6)	75/965 (8)
Anaplastic	4/954 (<0.5)	3/965 (<0.5)
Primary tumor stage		
pT1	157 (14)	162 (15)
pT2	868 (79)	882 (80)
pT3	71 (6)	52 (5)
Other[f]	5 (<0.5)	2 (<0.5)
Axillary nodal status[g]		
0	577 (52)	573 (52)
1–3	390 (35)	390 (36)
≥4	134 (12)	135 (12)
AJCC stage at surgery		
I[h]	4/1100 (<0.5)	1 (<0.5)
II	933/1100 (85)	940 (86)
III	163/1100 (15)	157 (14)
PD-L1 status[g]		
IC0	316 (29)	316 (29)
IC1–3	785 (71)	782 (71)
Surgery[g]		
Breast conserving	524 (48)	523 (48)
Mastectomy	577 (52)	575 (52)

Abbreviations: AJCC, American Joint Commission on Cancer; ECOG, Eastern Cooperative Oncology Group, where 0 represents fully active, able to carry on all pre-disease performance without restrictions and 1 represents restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature; PD-L1, programmed death-ligand 1.
[a] All entries are No. (%) unless otherwise noted.
[b] Native Hawaiian/other Pacific Islander (n = 1), multiple (n = 1).
[c] China, Hong Kong, Japan, Republic of Korea, Singapore, Taiwan, Thailand.
[d] Austria, Belgium, Czech Republic, Denmark, France, Germany, Hungary, Ireland, Israel, Italy, Poland, Romania, Spain, Switzerland, Turkey, Ukraine, United Kingdom.
[e] Argentina, Brazil, Mexico, Peru.
[f] Includes pT0, pTis, pT4, pT4b, and missing.
[g] As recorded in the interactive voice-/web-response system (iXRS).
[h] Not eligible for the trial.

Table 2. Summary of Primary and Secondary Efficacy End Points in the ITT Population

End Point	No. of Events (%)		Stratified[a] Hazard Ratio (95% CI)	3-Year Event-Free Percentage (standard error)		
	Atezolizumab + Chemotherapy (n = 1101)	Chemotherapy Alone (n = 1098)		Atezolizumab + Chemotherapy (n = 1101)	Chemotherapy Alone (n = 1098)	Difference (95% CI)
iDFS (primary)	141 (12.8)	125 (11.4)	1.11 (0.87 to 1.42)	84.6 (1.23)	86.4 (1.18)	–1.8 (–5.2 to 1.5)
iDFS, PD-L1 IC1–3	83/785 (10.6)	81/782 (10.4)	1.00 (0.73 to 1.35)	87.6 (1.31)	88.0 (1.32)	–0.4 (–4.0 to 3.2)
iDFS, node-positive TNBC	92/534 (17.2)	70/533 (13.1)	1.32 (0.97 to 1.80)	78.1 (2.10)	83.1 (1.93)	–5.0 (–10.6 to 0.6)
Overall survival	72 (6.5)	58 (5.3)	1.23 (0.87 to 1.73)	92.3 (0.93)	93.7 (0.85)	–1.3 (–3.8 to 1.2)
iDFS including second primary non-breast invasive cancer	144 (13.1)	135 (12.3)	1.05 (0.83 to 1.33)	84.4 (1.24)	85.3 (1.24)	–1.0 (–4.4 to 2.5)
Recurrence-free interval	119 (10.8)	113 (10.3)	1.04 (0.80 to 1.34)	86.7 (1.17)	87.7 (1.13)	–1.0 (–4.2 to 2.2)
Distant recurrence-free interval	86 (7.8)	88 (8.0)	0.97 (0.72 to 1.31)	90.0 (1.05)	90.3 (1.03)	–0.3 (–3.1 to 2.6)
Disease-free survival	145 (13.2)	135 (12.3)	1.06 (0.84 to 1.34)	84.3 (1.24)	85.3 (1.24)	–1.1 (–4.5 to 2.4)

Abbreviations: iDFS, invasive disease-free survival; PD-L1, programmed death-ligand 1; TNBC, triple-negative breast cancer

[a] Hazard ratios estimated by stratified Cox regression with the following strata: axillary nodal status, surgery (breast conserving vs mastectomy), and tumor PD-L1 status. Event-free rate based on Kaplan–Meier estimates.

Table 3. Most Common AEs (>15% of Patients) and Immune-Mediated AEs (>10% of Patients) in the Safety Population[a]

AE	Atezolizumab + Chemotherapy (n = 1093)		Chemotherapy Alone (n = 1084)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Most common AEs				
Alopecia	735 (67)	NA	715 (66)	NA
Nausea	553 (51)	8 (1)	531 (49)	12 (1)
Anemia	423 (39)	71 (6)	424 (39)	70 (6)
Fatigue	326 (30)	23 (2)	269 (25)	19 (2)
ALT increased	297 (27)	49 (4)	242 (22)	25 (2)
Diarrhea	287 (26)	15 (1)	188 (17)	1 (<0.5)
Neutrophil count decreased	279 (26)	172 (16)	260 (24)	163 (15)
Neutropenia	247 (23)	178 (16)	255 (24)	173 (16)
AST increased	247 (23)	27 (2)	161 (15)	7 (1)
WBC decreased	240 (22)	110 (10)	200 (18)	95 (9)
Asthenia	235 (22)	17 (2)	231 (21)	11 (1)
Constipation	231 (21)	2 (<0.5)	210 (19)	0
Arthralgia	218 (20)	1 (<0.5)	150 (14)	1 (<0.5)
Decreased appetite	214 (20)	11 (1)	145 (13)	4 (<0.5)
Myalgia	202 (18)	2 (<0.5)	175 (16)	3 (<0.5)
Peripheral sensory neuropathy	196 (18)	3 (<0.5)	185 (17)	1 (<0.5)
Vomiting	177 (16)	7 (1)	147 (14)	6 (1)
Headache	177 (16)	1 (<0.5)	135 (12)	0
Pyrexia	170 (16)	0	113 (10)	1 (<0.5)
Rash	170 (16)	8 (1)	89 (8)	1 (<0.5)
Hypothyroidism	163 (15)	2 (<0.5)	6 (1)	0
Immune-mediated AEs				
Rash	471 (43)	22 (2)	327 (30)	5 (<0.5)
Hepatitis (diagnosis and laboratory abnormalities)	370 (34)	66 (6)	286 (26)	30 (3)
Hepatitis (laboratory abnormalities)	354 (32)	59 (5)	281 (26)	28 (3)
Hepatitis (diagnosis)	23 (2)	7 (1)	8 (1)	2 (<0.5)
Hypothyroidism	205 (19)	3 (<0.5)	10 (1)	0

Table 3. Most Common AEs (>15% of Patients) and Immune-Mediated AEs (>10% of Patients) in the Safety Population[a]

AE	Atezolizumab + Chemotherapy (n = 1093)		Chemotherapy Alone (n = 1084)	
	Any grade	Grade 3/4	Any grade	Grade 3/4

Abbreviations: AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; NA, not applicable; WBC, white blood cell count.
[a] All entries are No. (%). AEs were graded using National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0.

Adjuvant Atezolizumab for Early Triple-Negative Breast Cancer: The ALEXANDRA/IMpassion030 Randomized Clinical Trial

Michail Ignatiadis, MD, et al.

Supplementary materials

Contents

eTable 1. List of Investigators

Country	Site Name	Principal Investigator	No. of Patients Randomized
Russian Federation (n = 367)	BIH at Omsk Region "Clinical Oncology Dispensary", Omsk	Anastasia Zimina	43
	Private Healthcare Institution Clinical Hospital RZhD Medicine, St. Petersburg	Aleksandr Vasiliev	41
	Regional Clinical Oncology Hospital, Prospect Oktyabrya 67, Yaroslavl	Nikolay Kislov	26
	FBI "Scientific Research Institute of Oncology n. a. N. N. Petrov", Saint Petersburg	Petr Krivorotko	22
	Arkhangelsk Regional Clinical Oncology Dispensary, Arhangelsk	Lyudmila Lebedeva	20
	Moscow Clinical Scientific Center, Moscow	Lyudmila Zhukova	19
	Regional Oncology Hospital, Irkutsk	Dmitry Ponomarenko	19
	Multidisciplinary Clinic Reaviz, Samara	Mikhail Kopp	18
	Regional Clinical Hospital, Saratov	Svetlana Averyanova	18
	Oncologica Dispensary #2, Sochi	Dmitry Kirtbaya	17
	P.A. Herzen Oncological Institute, Moscow	Larisa Bolotina	16
	Mordovia State University, Saransk	Pavel Skopin	16
	Ivanovo Regional Oncology Dispensary, Ivanovo	Evgeniy Gotovkin	13
	FSBI Russian Oncology Research Center n.a. Blokhin of MOH RF, Moscow	Elena Artamonova	13
	S-Pb Clinical Scientific Practical Center of Specialized Kinds of Medical Care (Oncological), Saint Petersburg	Vladimir Moiseenko	11
	National Medical Research Center for Oncology, Rostov	Lyubov Vladimirova	10
	SHI Volgograd Regional Clinical Oncological Dispensary#1, Volgograd	Nadezhda Kovalenko	7
	Regional Oncology Dispensary, Veliky Novgorod	Boris Frumkin	7
	Evimed, Chelyabinsk	Oleg Gladkov	6
	Nizhny Novgorod Regional Clinical Oncology Center, Nizhniy Novgorod	Irina Shumskaya	6
	Medsi Clinic, 6th km Pyatnitskoye Shosse, Moscow	Anastasia Mochalova	5
	LCC Center of Palliative Medicine - Devita, Saint Petersburg	Svetlana Uvarova	4
	Pyatigorsky Oncologic Dispensary, Stavropol	Vladimir Vladimirov	3
	Bashkirian Republican Clinical Oncology Dispensary, Ufa	Alsu Iskhakova	3
	EosMed LLC, Pesochniy, Saint Petersburg	Mikhail Kramchaninov	2
	LLC Strategic Medical Systems, Saint Petersburg	Sergey Orlov	1
	Samara Regional Oncology Dispensary, Samara	Yulia Makarycheva	1
Ukraine (n = 288)	Lviv State Oncological Regional Treatment and Diagnostic Center, Lviv	Yaroslav Shparyk	45
	Volyn Regional Oncology Dispensary, Lutsk	Ivan Sinielnikov	43
	Vinnytsya Regional Clinical Oncology Dispensary, Vinnytsya	Iryna Matsishevska	36
	Municipal Institution Odesa Regional Oncology Dispensary, Odesa	Yuliia Krasnohrud	33
	Regional Oncology Center, Chernigiv	Sergey Polenkov	29
	ME Kryviy Rih Oncology Dispensary of Dnipropetrovs'k Regional Council, Kryvyi Rih	Hryhoriy Adamchuk	27
	City Clinical Hospital #4, Dnipropetrovsk	Igor Bondarenko	24
	Transkarpathian Regional Oncology Clinic, Uzhgorod	Andriy Rusyn	11

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Country	**Site Name**	**Principal Investigator**	**No. of Patients Randomized**
	CCCH City Oncological Center SHEI Uzhgorod NU, Uzhgorod	Yevhen Hotko	10
	MI “Clinical Oncological Dispensary” of Dnipro Reg Council, Dnipro	Natalia Zvonarova	8
	Municipal Institution Odesa Regional Clinical Hospital, Odesa	Oleksandr Berzoy	7
	Chernivtsi Regional Clinical Oncology Dispensary, Chernivtsi	Anna Pidverbetska	6
	Sumy Reg. Clin. Oncological Dispensary, Sumy Region	Andriy Kurochkin	4
	Zaporizhzhia Regional Clinical Oncology Dispensary, Zaporizhia	Olexiy Kovalyov	3
	Yulis Medical and Diagnostic Center, Zaporizhzhia	Olexiy Kovalyov	1
	Municipal Institution Kirovograd Regional Oncology Dispensary, Kirovograd	Andrij Gardashnikov	1
China (n = 268)	Fudan University Shanghai Cancer Center, Shanghai	Zhimin Shao	62
	Henan Cancer Hospital, Zhengzhou	Zhenzhen Liu	29
	Harbin Medical University Cancer Hospital, Harbin	Qingyuan Zhang	23
	The First Affiliated Hospital of College of Medicine, Hangzhou	Peng Shen	15
	Fujian Medical University Union Hospital, Fuzhou	Chuan Wang	13
	West China Hospital, Sichuan University, Chengdu	Ting Luo	12
	Beijing Union Hospital, Beijing	Qiang Sun	11
	The Second Affiliated Hospital of Zhejiang University College, Hangzhou	Yongchuan Deng	9
	The First Hospital of Jilin University, Changchun	Zhimin Fan	9
	Beijing Hospital; Internal Medicine-Oncology, Beijing	Yongqiang Zhang	9
	Hebei Medical University Fourth Hospital, Shijiazhuang	Cuizhi Geng	8
	Jilin Cancer Hospital, Changchun	Ying Cheng	7
	Nanjing Drum Tower Hospital, the Affiliated Hospital of Nanjing University Medical School, Nanjing	Wenjing Hu	7
	Wuhan Union Hospital Tongji Medical College, Wuhan City	Jing Cheng	7
	Sun Yat-Sen University Cancer Center, Guangzhou	Shusen Wang	6
	Shandong Cancer Hospital, Jinan	Yongsheng Wang	5
	Peking University People’s Hospital, Beijing	Shu Wang	5
	Shanghai Jiao Tong University School of Medicine (SJTUSM) - Ruijin Hospital (GuangCi Hospital), Shanghai	Kunwei Shen	4
	Zhejiang Cancer Hospital, Hangzhou City	Hongjian Yang	4
	Luoyang Central Hospital, Luoyang City	Mingli Ni	4
	The University of Hong Kong-Shenzhen Hospital, Shenzhen City	Zhiyuan Xu	4
	The First Affiliated Hospital of Xian Jiao Tong University, Xi’an City	Jin Yang	3
	The 900th Hospital of PLA Joint Service Support Force, Fuzhou	Xi Chen	3
	Zhongshan Hospital Fudan University, Shanghai City	Hongwei Zhang	3
	Chongqing Cancer Hospital, Chongqing City	Xiaohua Zeng	3
	Guangdong General Hospital, Guangzhou	Ning Liao	2
	Hubei Cancer Hospital, Wuhan	Xinhong Wu	1
Japan (n = 249)	Kanagawa Cancer Center, Kanagawa	Toshinari Yamashita	34
	Osaka International Cancer Institute, Osaka	Takahiro Nakayama	25
	Chiba Cancer Center, Chiba	Rikiya Nakamura	20
	Saitama Cancer Center, Saitama	Kenichi Inoue	18
	The Cancer Institute Hospital of JFCR, Tokyo	Toshimi Takano	15
	Saitama Medical University International Medical Center, Saitama	Hiroshi Ishiguro	13

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Country	**Site Name**	**Principal Investigator**	**No. of Patients Randomized**
	Aichi Cancer Center Hospital, Aichi	Hiroji Iwata	10
	Hyogo Medical University Hospital, Hyogo	Yasuo Miyoshi	10
	Tokai University Hospital, Kanagawa	Naoki Niikura	10
	Naha-nishi Clinic, Okinawa	Yoshihiko Kamada	10
	Sagara Hospital, Kagoshima	Tetsuhiko Taira	10
	National Hospital Organization Kyushu Cancer Center, Fukuoka-shi	Eriko Tokunaga	10
	Kyoto University Hospital, Kyoto	Kosuke Kawaguchi	10
	Shikoku Cancer Center, Ehime	Daisuke Takabatake	10
	Shizuoka Cancer Center, Shizuoka	Tomomi Hayashi	9
	University of Tsukuba Hospital, Ibaraki	Hiroko Bando	6
	National Hospital Organization Osaka National Hospital, Osaka	Hiroyuki Yasojima	6
	National Hospital Organization Hokkaido Cancer Center, Hokkaido	Nobumoto Tomioka	6
	Hiroshima City Hiroshima Citizens Hospital, Hiroshima	Mitsuya Itoh	6
	Fukushima Medical University Hospital, Fukushima	Shigehira Saji	5
	St. Luke's International Hospital, Tokyo	Atsushi Yoshida	4
	Okayama University Hospital, Okayama	Tsuguo Iwatani	2
Republic of Korea (n = 158)	Soon Chun Hyang University Cheonan Hospital	Han Jo Kim	21
	Asan Medical Center, Seoul	Sung-Bae Kim	14
	Gachon University Gil Medical Center, Incheon	Hee Kyung Ahn	14
	Samsung Medical Center, Seoul	Ji-Yeon Kim	13
	Seoul National University Hospital, Seoul	Seock Ah Im	12
	Seoul National University Bundang Hospital, Seongnam-si	Jee Hyun Kim	10
	Ajou University Hospital, Suwon	Seok Yun Kang	10
	Seoul St Mary's Hospital, Seoul	Ji Eun Lee	10
	Severance Hospital, Seoul	Joo Hyuk Sohn	9
	Chungbuk National University Hospital, Cheongju-si	Ki Hyeong Lee	9
	National Cancer Center, Kyunggi-Do	Keun Seok Lee	8
	Ulsan University Hospital, Ulsan	Su Jin Koh	8
	Ewha Womans University Mokdong Hospital, Seoul	Kyoung Eun Lee	7
	CHA Bundang Medical Center, Seongnam-si	Yong Wha Moon	4
	Gangnam Severance Hospital, Seoul	Jee Hung Kim	4
	Inha University Hospital, Incheon	Moon Hee Lee	4
	Wonju Christian Hospital, Seoul	Seung Taek Lim	1
France (n = 143)	Clinique Tivoli; Sce Radiotherapie, Bordeaux	Nathalie Bonichon Lamichhane	14
	CRLCC-Francois Baclesse, Caen	Christelle Levy	12
	Centre Georges Francois Leclerc, Dijon	Sylvain Ladoire	11
	Clinique Clémentville, Montpellier	Ivan Toledano	10
	Institut du Cancer Coulancy Reims, Reims	Karinne Prulhiere	8
	Centre Henri Becquerel, Rouen	Jean Christophe Thery	7
	Hopital Prive Jean Mermoz, Lyon	Olfa Derbel	7
	Hopital Prive Drome Ardeche, Valence	Louis Doublet	6
	Centre Antoine Lacassagne, Nice	Jean-Marc Ferrero	5
	l'Hôpital Privé du Confluent SAS, Nantes	Alain Lortholary	5
	Institut Gustave Roussy, Villejuif	Barbara Pistilli	5
	CH de Beauvais, Beauvais	Hanifa Ammarguellat	5
	Institut Claudius Régaud, Toulouse	Florence Dalenc	4
	Centre Hospitalier Regional Metz-Thionville - Hopital de Mercy, Vandoeuvre-Les-Nancy	Elisabeth Luporsi	4
	Centre Hospitalier Departemental de Vendee, La Roche Sur Yon	Frank Priou	3
	Clinique Chenieux, Limoges	Dominique Genet	3
	Centre Hospitalier Bretagne Sud, Lorient	Regine Lamy	3

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Country	**Site Name**	**Principal Investigator**	**No. of Patients Randomized**
	Institut de Cancérologie de Lorraine, Vandoeuvre-Les-Nancy	Vincent Massard	3
	CH de Cholet, Cholet	Victor Simmet	3
	Centre Hospitalier Fleyriat, Bourg en Bresse	Hubert Orfeuvre	2
	Centre Paul Strauss, Strasbourg	Thierry Petit	2
	Polyclinique Bordeaux Nord Aquitaine, Bordeaux	Nadine Dohollou	2
	CHU Jean Minjoz, Besancon	Loic Chaigneau	2
	Institut Sainte Catherine, Avignon	Julien Grenier	2
	Institut Jean Godinot, Reims	Christelle Jouannaud	2
	Institut Régional du Cancer Montpellier, Montpellier	William Jacot	2
	Chi De Cornouaille, Quimper	Delphine Mollon Grange	2
	Hopitaux Du Leman - Site Georges Pianta, Thonon Les Bains	Andreea Ciobanu	2
	Institut De Cancerologie Lucien Newrth, St-Priest-En-Jarez	Pierre Fournel	1
	CHRU De Brest - Hopital Morvan - Institut De Cancerologie Et D'Hematologie, Brest	Helene Simon	1
	CH Annecy Genevois Site Annecy, Metz Tessy	Laetitia Stefani	1
	Centre Hospitalier Alpes Leman, Contamine Sur Arve	Mansour Rastkhah	1
	Hôpital Saint Joseph, Marseille	Cyril Foa	1
	CHU Tours - Hôpital Bretonneau, Tours	Marie-Agnes By	1
	Centre Hospitalier de Compiegne, Compiegne	Riccardo Samaritani	1
Spain (n = 75)	Hospital Universitario Virgen de Arrixaca, Murcia	Jose Luis Alonso	12
	Hospital Universitario de Canarias, La Laguna	Josefina Cruz Jurado	8
	Complexo Hospitalario de Vigo, Hospital Álvaro Cunqueiro, Vigo	Isabel Lorenzo	6
	Hospital Quirón Sagrado Corazón, Sevilla	Juan Carlos Quero	4
	Instituto Valenciano Oncologia, Valencia	Angel Guerrero Zotano	3
	Hospital Universitari Germans Trias i Pujol, Barcelona	Beatriz Cirauqui Cirauqui	3
	Hospital Clinico Universitario de Valencia, Valencia	Begona Bermejo De Las Heras	3
	Hospital General De Catalunya; Barcelona	Xavier Gonzalez Farre	3
	Hospital Universitari Sant Joan de Reus, Tarragona	Cinta Albacar	3
	Hospital Universitario de Fuenlabrada, Madrid	Laura Rodriguez Lajusticia	3
	Centro Oncologico de Galicia COG, La Coruña	Manuel Ramos Vazquez	2
	Complejo Hospitalario Universitario de Santiago (CHUS), La Coruña	Rafael Lopez Lopez	2
	Hospital Universitario de Burgos, Burgos	Blanca Hernando Fernandez De Aranguiz	2
	Hospital General Universitario de Valencia, Valencia	Vega Iranzo Gonzalez Cruz	2
	Centro Integral Oncológico Clara Campal Ensayos Clínicos START, Madrid	Beatriz Rojas	2
	Consorci Hospitalari de Terrassa, Barcelona	Maria Marin Alcala	2
	Hospital Clinico Universitario Virgen de la Victoria, Malaga	Maria Emilia Dominguez	2
	Hospital Son Llatzer, Palma de Mallorca	Aida Bujosa Rodriguez	2
	Complejo Hospitalario de Jaen, Jaen	Pedro Sanchez Rovira	1
	Hospital Clinico Universitario Lozano Blesa, Zaragoza	Pilar Bueso Inglan	1

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Country	**Site Name**	**Principal Investigator**	**No. of Patients Randomized**
	Hospital San Pedro De Alcantara, Caceres	Santiago Gonzalez Santiago	1
	Hospital Provincial Castellón, Castellón	Eduardo Martinez De Dueñas	1
	Hosp Univ Fundacion Alcorcon, Madrid	Clara Olier Garate	1
	Complejo Asistencial Universitario de Leon, Leon	Ana Lopez	1
	Hospital Universitario Ramón y Cajal, Madrid	Elena Lopez Miranda	1
	Hospital General Universitario Gregorio Marañon, Madrid	Miguel Martin	1
	Hospital Universitario Puerta de Hierro - Majadahonda, Madrid	Blanca Cantos	1
	Hospital de Jerez, Cadiz	Natalia Chavarria	1
	Hospital Infanta Sofia, Madrid	Maria Merino Salvador	1
Mexico (n = 74)	IEM-FUCAM, Mexico City	Flavia Morales-Vasques	18
	Centro Médico Zambrano Hellion, San Pedro Garza García	Servando Cardona Huerta	14
	Oncologico Potosino, Mariano Arista 965, San Luis Potosí	Jessica Reyes Contreras	14
	Centro Medico Dalinde, Mexico City	Ricardo Villalobos Valencia	10
	Dentro De Condominio San Francisco	Alejandro Juarez Ramiro	7
	Merida | Investigacion Clinica, Mérida	Jaime Alejandro Tec Chan	5
	Instituto Nacional De Cancerologia, Mexico City	Paula Anel Cabrera Galeana	2
	Centro de Investigacion Clinica de Oaxaca, Oaxaca de Juárez	Yolanda Lizbeth Bautista Aragon	2
	Health Pharma Professional Research, Mexico City	Fabian Martinez	2
Italy (n = 73)	Istituto Europeo Di Oncologia, Milano	Marco Angelo Colleoni	16
	Azienda Ospedaliera di Perugia Ospedale S. Maria della Misericordia, Perugia	Anna Maria Mosconi	12
	Azienda Ospedaliero Universitaria San Martino, Genova	Alberto Ballestrero	5
	Nuovo Ospedale Di Prato, Prato	Laura Biganzoli	4
	Ospedale degli Infermi, Rimini	Lorenzo Gianni	4
	Policlinico San Mattea, Pavia	Paolo Pedrazzoli	4
	Istituto Clinico Humanitas, Rozzano	Armando Santoro	3
	Azienda Ospedaliero - Universitaria di Modena Policlinico, Modena	Luca Moscetti	3
	A.O. Universitaria S. Maria Della Misericordia Di Udine, Udine	Alessandro Minisini	3
	Asst Di Lecco, Lecco	Antonio Ardizzoia	3
	Azienda Ospedaliera SS. Antonio E. Biagio E. Cesare Arrigo di Alessandria, Alessandria	Maura Vincenti	3
	Azienda Ospedaliero Universitaria di Parma, Parma	Antonino Musolino	2
	Azienda Usl 7, Poggibonsi	Angelo Martignetti	2
	Azienda Ospedaliera Papa Giovanni XXIII, Bergamo	Carlo Alberto Tondini	1
	Policlinico Universitario Campus Biomedico Di Roma, Roma	Giuseppe Tonini	1
	Ospedale Degli Infermi – Faenza, Lugo	Stefano Tamberi	1
	U.O Medicina Oncologica Ospedale di Carpi, Carpi	Katia Cagossi	1
	Azienda Ospedaliero Universitaria Di Bologna - Policlinico S.Orsola Malpighi, Bologna	Claudio Zamagni	1
	Ospedale Santa Maria Annunziata, Bagno A Ripoli	Francesca Martella	1

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Country	**Site Name**	**Principal Investigator**	**No. of Patients Randomized**
	Ospedale Degli Infermi Di Biella, Biella	Elena Seles	1
	Ospedale Mater Salutis, Legnago	Anna Mercanti	1
	Fondazione Salvatore Maugeri, Pavia	Raffaella Palumbo	1
Taiwan (n = 70)	National Cheng Kung University Hospital, Tainan	Wei-Pang Chung	15
	National Taiwan University Hospital, Taipei	Chiun-Sheng Huang	14
	Taipei Veterans General Hospital, Taipei City	Ling-Ming Tseng	14
	Kaohsiung Medical University Hospital, Kaohsiung	Ming-Feng Hou	12
	Tri-Service General Hospital, Taipei	Jyh-Cherng Yu	5
	Chi Mei Medical Center Liou Ying Campus, Liouying District	Wen-Tsung Huang	4
	Chunghua Christian Hospital, Changhua	Hung-Wen Lai	3
	Chang Gung Medical Foundation Linkou Branch, Taipei	Shin-Cheh Chen	1
	E-Da Cancer Hospital, Kaohsung	Kun-Ming Rau	1
	Mackay Memorial Hospital - Taipei Branch, Taipei	Yuan-Ching Chang	1
Brazil (n = 58)	Crio - Centro Regional Integrado De Oncologia, Floresta	Eduardo Henrique Silva	9
	Instituto Brasileiro De Controle Do Câncer – São Camilo Oncologia, Sao Paulo	Felipe Jose Cruz	8
	Hospital de Cancer de Barretos, Barretos	Cristiano Souza	8
	Clinica de Neoplasias Litoral, Itajai	Giuliano Borges	7
	Hospital Mae de Deus, Porto Alegre	Christina Oppermann	5
	Oncosite - Centro De Pesquisa Clinica Em Oncologia Ltda, Ijui	Fabio Andre Franke	4
	Hospital Moinhos de Vento, Porto Alegre	Daniela Rosa	3
	Faculdade de Medicina do ABC - FMABC, Santo Andre	Daniel Cubero	3
	Instituto Do Câncer Do Estado de São Paulo Octávio Frias de Oliveira, São Paulo	Paola Pinto	3
	Instituto Nacional de Cancer – INCa, Rio de Janeiro	Jose Bines	2
	Hospital Jardim Amália, Volta Redonda	Heloisa Resende	2
	Nucleo de Oncologia da Bahia - NOB, Salvador	Luciana Landeiro	2
	Hospital das Clinicas - UFRGS, Porto Alegre	Pedro Emanuel Liedke	1
	Hospital Amaral Carvalho, Jau	Patricia Beato	1
Thailand (n = 56)	Songklanagarind Hospital, Songkla	Patrapim Sunpaweravong	19
	Ramathibodi Hospital; Medicine/Oncology, Bangkok	Thitiya (Sirisinha) Dejthevaporn	12
	Srinagarind Hospital, Khon Kaen University, Khon Kaen	Ongart Somintara	10
	Siriraj Hospital; Clinical Research Center, Bangkok	Suthinee Ithimakin	9
	King Chulalongkorn Memorial Hospital, Bangkok	Napa Parinyanitikul	4
	Rajavithi Hospital, Bangkok	Piyawan Tienchaianada	1
	Lampang Cancer Hospital, Muang Lampang	Sirikul Sorrarittichingchai	1
Germany (n = 52)	Universitätsklinik Tübingen, Tübingen	Eva-Maria Grischke	9
	Onkodok GmbH, Gütersloh	Reinhard Depenbusch	6
	Universitätsmedizin Mainz, Klinik u. Poliklinik f. Geburtshilfe u. Frauenheilkunde, Mainz	Marcus Schmidt	5
	Onkozentrum Dres. Göhler, Dresden	Thomas Goehler	4
	Klinikum Worms, Worms	Matthias Koegel	4
	Marien-Hospital Witten, Witten	John Hackmann	3
	Johannes Wesling Klinikum Minden, Minden	Martin Griesshammer	3
	Johanniter Frauenklinik Stendal Germany, Stendal	Andrea Stefek	3

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Country	**Site Name**	**Principal Investigator**	**No. of Patients Randomized**
	Klinikum Ludwigsburg, Ludwigsburg	Claudia Hanle	3
	St. Vincenz-Elisabeth-Hospital; Katholisches Klinikum Mainz, Mainz	Arnd Honig	3
	Klinikum Memmingen, Memmingen	Felix Flock	2
	Klinikum der Universität München, München	Nadia Harbeck	1
	Ärztehaus am Bahnhofsplatz; Praxis Uleer/Pourfard, Hildesheim	Christoph Uleer	1
	St. Johannes-Hospital, Dortmund	Georg Kunz	1
	Gynäkologie Kompetenzzentrum, Stralsund	Carsten Hielscher	1
	BAG Freiberg-Richter, Jacobasch, Dresden	Thomas Illmer	1
	St. Elisabeth-Krankenhaus, Köln	Susanne Brandner	1
	Albertinen-Krankenhaus Klinik f. Gynäkologie und Geburtshilfe, Hamburg	Ulrike Dorste	1
United States (n = 31)	Baptist - MD Anderson Cancer Center, Jacksonville, FL	Dayra Avila-Lima	6
	Cancer Center of Kansas, Wichita, KS	Shaker Dakhil	4
	Memorial Sloan Kettering Cancer Center, New York, NY	Tiffany Traina	4
	SCRI, Nashville, TN	Erika Hamilton	3
	Rochester General Hospital, Rochester, NY	Farhan Imran	3
	New Hampshire Hematology Oncology, Hooksett, NH	Douglas Weckstein	2
	University of Maryland Greenebaum Comprehensive Cancer Center, Baltimore, MD	Paula Rosenblatt	2
	Monter Cancer Center, Lake Success, NY	Ruby Sharma	2
	Des Moines Oncology Research Association, Des Moines, IA	Seema Harichand-Herdt	2
	John Muir Health Clinical Research Center, Concord, CA	Gigi Chen	1
	Cedars-Sinai Medical Center, Los Angeles, CA	Monica Mita	1
	St. Mary's Medical Center, Huntington, WV	Arvinder Bir	1
Australia (n = 27)	Monash Medical Centre, East Bentleigh	Marion Harris	4
	Macquarie University Hospital, Westmead	Dhanusha Sabanathan	4
	Austin Hospital Olivia Newton John Cancer Centre, Heidelberg	Shane White	3
	Wesley Medical Centre, Auchenflower	Nicole Mccarthy	3
	Ashford Cancer Center Research, Kurralta Park	Kerry Cheong	3
	Royal Adelaide Hospital, Adelaide	Sudarshan Selva-Nayagam	2
	Sydney Adventist Hospital, Wahroonga	Joseph Rutovitz	2
	Princess Alexandra Hospital, Chermside	Kate Cuff	2
	Lismore Base Hospital, Lismore	Adam Boyce	1
	Mater Hospital, South Brisbane	Kathryn Middleton	1
	St Vincent's Hospital Sydney, Darlinghurst	Elgene Lim	1
	Maroondah Hospital, Ringwood East	Laura Pellegrini	1
Belgium (n = 26)	AZ Klina, Brasschaat	Didier Verhoeven	6
	UZ Leuven Gasthuisberg, Leuven	Benoit Beuselinck	4
	Institut Jules Bordet, Brussels	Michail Ignatiadis	4
	Vitaz, Sint Niklaas	Ines Deleu	3
	Clinique Sainte-Elisabeth, Namur	Stephanie Henry	3
	CHC MontLégia, Boulevard Patience et Beaujonc, Liege	Marie-Pascale Graas	3
	CHR de la Citadelle, Liège	Jean-Paul Salmon	2
	CHU Ambroise Paré, Mons	Vinciane Casert	1
Denmark (n = 22)	Sygehus Lillebælt, Vejle, Vejle	Else Maae	10
	Odense Universitetshospital, Onkologisk Afdeling, Odense	Jeanette Dupont Jensen	9
	Herlev Hospital; Afdeling for Kræftbehandling, Herlev	Dorte Lisbet Nielsen	3
	Centrul de Oncologie Sfantul Nectarie, Craiova	Michael Schenker	15

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Country	**Site Name**	**Principal Investigator**	**No. of Patients Randomized**
Romania (n = 21)	"Filantropia" Clinical Hospital, Bucharest	Dragos Median	5
	Institutul Oncologic Prof. Dr. Ion Chiricuta Cluj Napoca, Cluj-Napoca	Nicoleta Antone	1
Argentina (n = 17)	Clinica Universitaria Reina Fabiola, Cordoba	Santiago Bella	3
	Hospital Britanico de Buenos Aires, C.A.B.A.	Ernesto Korbenfeld	3
	Instituto de Oncología de Rosario, Rosario	Cristian Micheri	3
	Centro Oncologico Riojano Integral (CORI), La Rioja	Diego Kaen	3
	Centro de Investigacion Clinica - Clinica Viedma S.A., Viedma	Ruben Dario Kowalyszyn	2
	Centro Medico San Roque, Tucuman	Juan Jose Zarba	1
	Centro de Oncologia e Investigacion Buenos Aires - COIBA, Buenos Aires	Mirta Varela	1
	Fundación Ars Medica, Jujuy	Alejandro Salvatierra	1
Ireland (n = 17)	Beaumont Hospital; Cancer Clinical Trials Unit, Beaumont Hospital, Dublin	Patrick Morris	13
	Mater Misericordiae University Hospital, Dublin	Austin Duffy	4
Hong Kong (n = 14)	Queen Elizabeth Hospital Department of Clinical Oncology, Kowloon	Wang Kwong Ho	8
	Pamela Youde Nethersole Eastern Hospital, Hong Kong	Sung Inda Soong	3
	Queen Mary Hospital, Hong Kong	Joanne Wing Yan Chiu	3
Poland (n = 14)	Instytut MSF Sp. z o.o., Lodz	Ewa Kalinka	5
	Wojskowy Instytut Medyczny - Panstwowy Instytut Badawczy, Warszawa	Renata Duchnowska	4
	MedPolonia, Poznan	Rodryg Ramlau	3
	Wielkopolskie Centrum Onkologi, Poznan	Maria Litwiniuk	2
Israel (n = 12)	Hadassah Med Org Kiryat, Kiryat Hadassah	Beatrice Uziely	3
	Rabin MC; Davidof Center - Oncology Institute, Petach Tikva	Rinat Yerushalmi	3
	The Chaim Sheba Medical Center, Tel Hashomer	Einav Gal-Yam	2
	Meir Medical center, Pediatrics, Tel Hashomer	Iryna Kuchuk	2
	Shaare Zedek Medical Center, Jerusalem	Hadar Goldvaser	2
Czech Republic (n = 12)	Fakultni Poliklinika Vseobecne Fakultni Niemocnice, Praha 2	Martina Zimovjanova	7
	Nemocnice Horovice, NH Hospital a.s., Hořovice	Martin Smakal	4
	Krajska nemocnice T. Bati, a.s., Zlin	Marketa Pospiskova	1
United Kingdom (n = 11)	The Christie NHS Foundation Trust, Manchester	Anne Armstrong	3
	Calderdale and Huddersfield NHS Foundation Trust, Huddersfield	Jo Dent	3
	University Hospitals of North Midlands NHS Trust-Royal Stoke University Hospital, Stoke on Trent	Daljit Gahir	2
	Nottingham University Hospitals NHS Trust - City Hospital, Nottingham	Sarah Khan	1
	NHS Lothian - Western General Hospital, Edinburgh	Olga Oikonomidou	1
	Leeds Teaching Hospital NHS Trust, St James's Institute of Oncology, Leeds	Rohan Iype	1
Peru (n = 10)	Instituto Nacional de Enfermedades Neoplasicas, Lima	Carlos Castañeda	6
	Oncosalud Sac, Lima	Henry Gomez-Moreno	3
	Hospital Nacional Carlos Alberto Seguin Escobedo-Essalud, Arequipa	Hernan David Moron Escobar	1
Austria (n = 10)	Salzkammergut-Klinikum Voecklabruck, Vöcklabruck	Ferdinand Haslbauer	3
	Medical University Innsbruck, Innsbruck	Daniel Egle	3
	Klinikum Kreuzschwestern Wels, Wels	Sonja Heibl	2
	AKH - Medizinische Universität Wien, Wien	Rupert Bartsch	1
	Ordensklinikum Linz Barmherzige Schwestern, Linz	Renate Pusch	1

eTable 1. List of Investigators			
Country	**Site Name**	**Principal Investigator**	**No. of Patients Randomized**
Switzerland (n = 8)	Brust-Zentrum Zürich, Zürich	Urs Breitenstein	6
	Hirslanden Medical Center - Tumorzentrum, Aarau	Andreas Jakob	1
	Centre Hospitalier Universitaire Vaudois - Lausanne, Lausanne	Khalil Zaman	1
Hungary (n = 7)	National Institute of Oncology, Budapest	Gabor Rubovszky	4
	Pécsi Tudományegyetem, Pécs	Laszlo Csaba Mangel	2
	Borsod-Abaúj-Zemplén Megyei Központi Kórház és Egyetemi Oktatókórház, Miskolc	Gergely Dombovari	1
Turkey (n = 6)	Mersin Universitesi Tip Fakultesi Hastanesi, Mersin	Emel Sezer	2
	Uludag Universitesi - Saglik Uygulama ve Arastirrma Merkezi, Bursa	Turkkan Evrensel	1
	Baskent Universitesi Adana Dr. Turgut Noyan Uygulama ve Arastirma Merkezi, Adana	Ozgur Ozyilkan	1
	Izmir Ekonomi Universitesi Medical Park Hastanesi, Izmir	Cagatay Arslan	1
	Medikal Park Samsun, Mimarsinan Mahallesi, Samsun	Dilek Erdem	1
Singapore (n = 3)	National University Hospital, Singapore	Soo Chin Lee	2
	National Cancer Centre, Singapore	Rebecca Dent	1

eTable 2. Primary End Point Sensitivity Analyses (ITT patients)

Sensitivity Analysis	Hazard Ratio (95% CI)	Log-rank p-value
For non-protocol therapy	No observations met criteria	
For stratification based on eCRF		
Stratified analysis	1.09 (0.83–1.45)	0.53
Unstratified analysis	1.12 (0.88–1.43)	0.34
For Ukraine crisis		
Stratified analysis	1.05 (0.82–1.35)	0.70
Unstratified analysis	1.07 (0.83–1.38)	0.60

Abbreviations: eCRF, electronic case report form.

eTable 3. Summary of Safety and Treatment Exposure in the Safety Population[a]

Parameter	Atezolizumab + Chemotherapy (n = 1093)	Chemotherapy Alone (n = 1084)
Any AE	1090 (100)	1074 (99)
Treatment-related AE, any grade	1085 (99)	1069 (99)
Treatment-related grade 3/4 AE	593 (54)	477 (44)
Treatment-related serious AE	208 (19)	110 (10)
Treatment-related grade 5 AE	0	1 (<0.5)
AE leading to any treatment discontinuation	192 (18)	63 (6)
Atezolizumab	146 (13)	–
Epirubicin	30 (3)	12 (1)
Doxorubicin	15 (1)	18 (2)
Cyclophosphamide	44 (4)	30 (3)
Paclitaxel	58 (5)	35 (3)
Treatment duration, days, median (IQR)		
Atezolizumab	351 (286–358)	–
Epirubicin	43 (43–50)	43 (43-49)
Doxorubicin	43 (43–48)	43 (43-49)
Cyclophosphamide	43 (43–49)	43 (43-49)
Paclitaxel	78 (78–85)	78 (78–85)
Dose intensity, %, mean (SD)		
Atezolizumab	96 (12)	–
Epirubicin	99 (8)	100 (4)
Doxorubicin	99 (8)	99 (6)
Cyclophosphamide	99 (8)	100 (3)
Paclitaxel	99 (6)	99 (6)

Abbreviations: AE, adverse event; IQR, interquartile range; SD, standard deviation.
[a] All entries are No. (%) unless otherwise noted.

eTable 4. Details of Adverse Events with Fatal Outcome by Patient

Adverse Event	Onset Day	Treatment Phase	Attributed to Study Drug
Atezolizumab + Chemotherapy			
COVID-19	26	Induction	No
COVID-19 pneumonia	100	Induction	No
Myocardial ischemia	107	Induction	No
COVID-19 pneumonia	120	Induction	No
COVID-19	140	Induction	No
Death[a]	167	Maintenance	No
Death[a]	206	Induction	No
Myocardial ischemia	209	Maintenance	No
Death[a]	301	Maintenance	No
Chemotherapy Alone			
Pneumonia	99	Induction	Yes (paclitaxel)
Cerebrovascular accident	119	Induction	No
Acute cardiac failure	125	Induction	No
COVID-19	146	Induction	No
Mesenteric artery thrombosis	175	Maintenance	No
Septic shock	180	Induction	No

[a] Unexplained death with no available information on the clinical course or laboratory parameters. An autopsy was not performed.

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eTable 5. Immune-Mediated Adverse Events by Treatment Period in the Safety Population

Immune-Mediated AEs	Induction Period		Overall	
	Atezolizumab + Chemotherapy (n = 1093)	Chemotherapy Alone (n = 1084)	Atezolizumab + Chemotherapy (n = 1 093)	Chemotherapy Alone (n = 1084)
Rash	431 (39)	325 (30)	471 (43)	327 (30)
Hepatitis (diagnosis and laboratory abnormalities)	321 (29)	279 (26)	370 (34)	286 (26)
Hepatitis (laboratory abnormalities)	308 (28)	275 (25)	354 (32)	281 (26)
Hepatitis (diagnosis)	17 (2)	6 (1)	23 (2)	8 (1)
Hypothyroidism	101 (9)	9 (1)	205 (19)	10 (1)
Hyperthyroidism	31 (3)	3 (<0.5)	63 (6)	3 (<0.5)
Pneumonitis	27 (2)	16 (1)	54 (5)	19 (2)
Adrenal insufficiency	16 (1)	0	30 (3)	0
Diabetes mellitus	8 (1)	3 (<0.5)	11 (1)	3 (<0.5)
Colitis	7 (1)	1 (<0.5)	10 (1)	1 (<0.5)
Pancreatitis	6 (1)	4 (<0.5)	8 (1)	4 (<0.5)
Hypophysitis	11 (1)	0	15 (1)	0
Ocular inflammatory toxicity	5 (<0.5)	2 (<0.5)	7 (1)	3 (<0.5)
Pericardial disorder	3 (<0.5)	2 (<0.5)	7 (1)	2 (<0.5)
Vasculitis	5 (<0.5)	6 (1)	6 (1)	6 (1)
Myocarditis	0	0	6 (1)	0

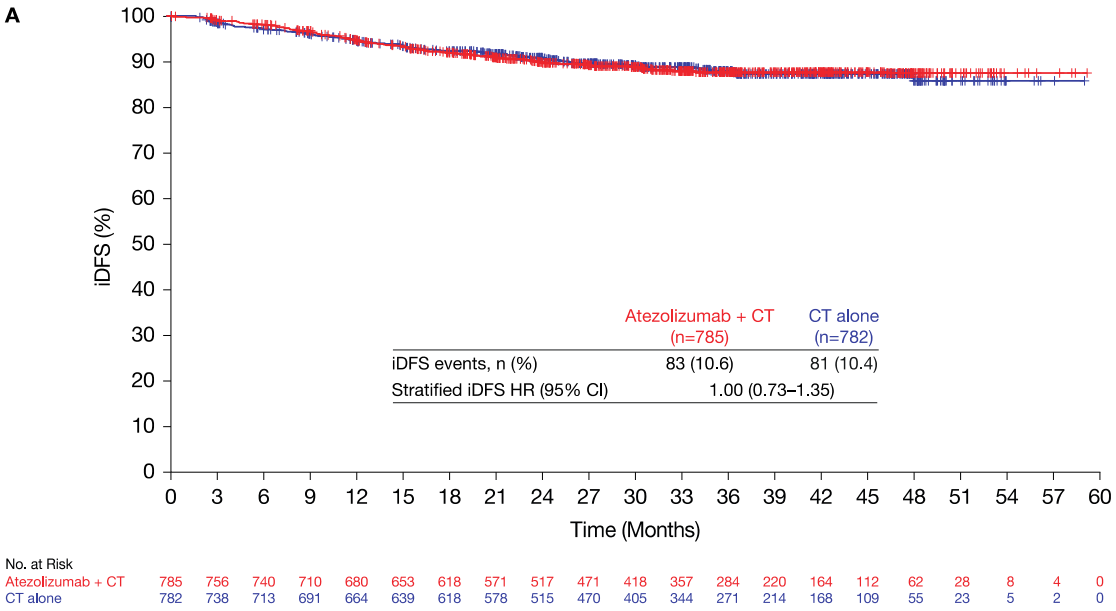
eTable 5. Immune-Mediated Adverse Events by Treatment Period in the Safety Population

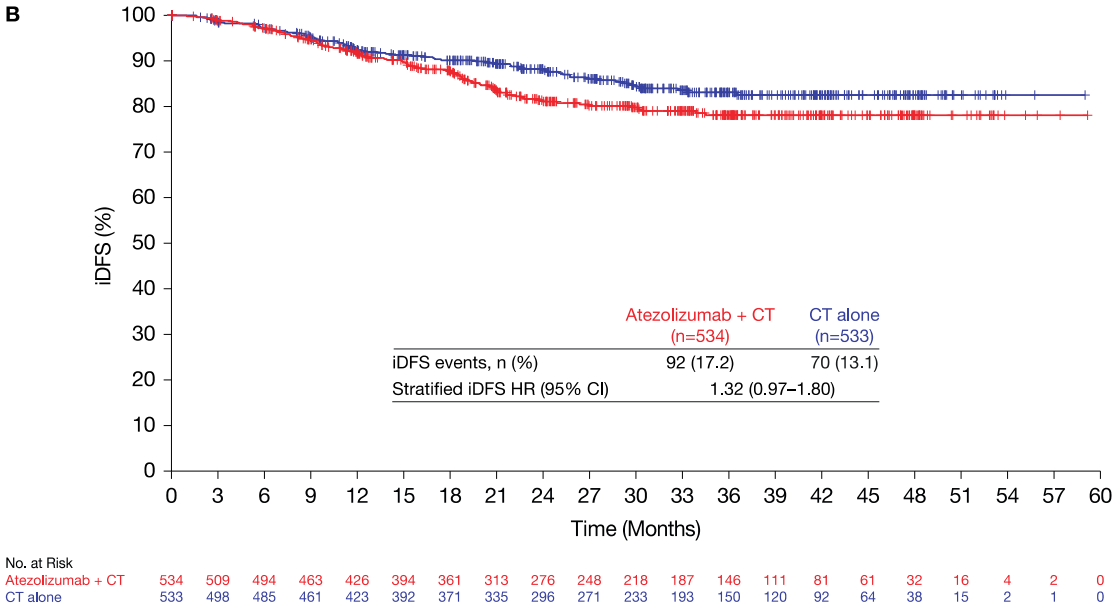
Immune-Mediated AEs	Induction Period		Overall	
	Atezolizumab + Chemotherapy (n = 1093)	Chemotherapy Alone (n = 1084)	Atezolizumab + Chemotherapy (n = 1 093)	Chemotherapy Alone (n = 1084)
Meningoencephalitis	4 (<0.5)	0	5 (<0.5)	0
Myositis	2 (<0.5)	0	4 (<0.5)	0
Nephritis	2 (<0.5)	0	3 (<0.5)	0
Severe cutaneous reaction	3 (<0.5)	1 (<0.5)	3 (<0.5)	1 (<0.5)
Autoimmune hemolytic anemia	0	1 (<0.5)	1 (<0.5)	1 (<0.5)

Abbreviation: AE, adverse event.
There were no cases of facial paresis, Guillain-Barré syndrome, hemophagocytic lymphohistiocytosis, myelitis, or myasthenia gravis in either treatment group.
[a] All entries are No. (%).

eFigure 1. Final Analysis of iDFS in Key Subgroups. A) PD-L1-Positive TNBC. B) Node-Positive TNBC

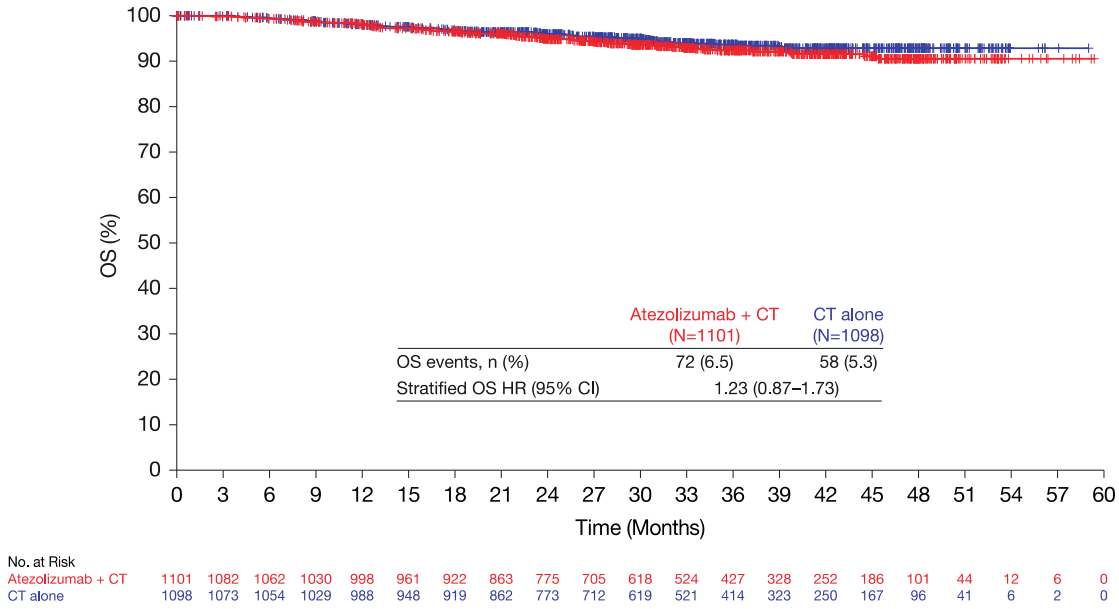
Abbreviations: CT, chemotherapy; HR, hazard ratio; iDFS, invasive disease-free survival; PD-L1, programmed death ligand 1; TNBC, triple-negative breast cancer.

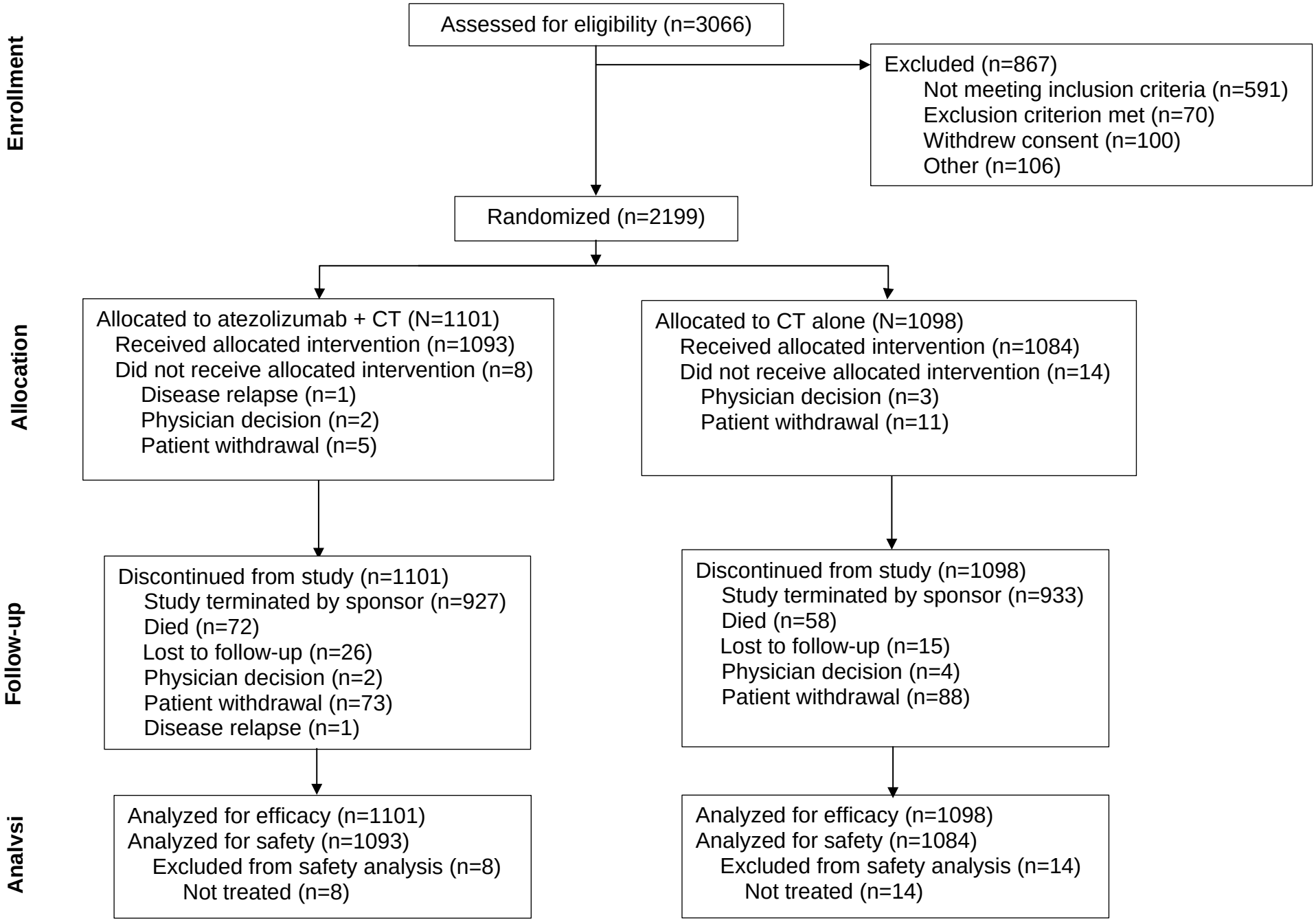


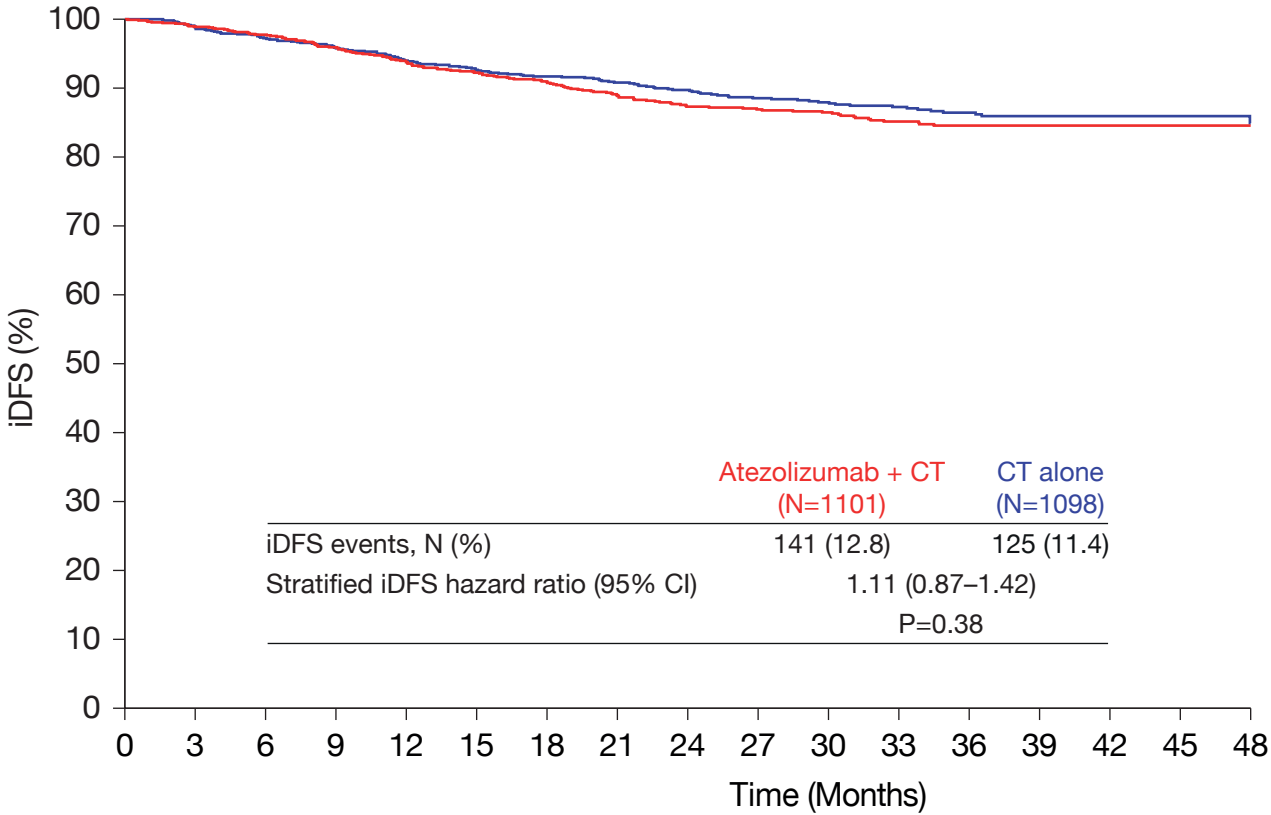


eFigure 2. Overall Survival

Abbreviations: CT, chemotherapy; HR, hazard ratio; OS, overall survival.

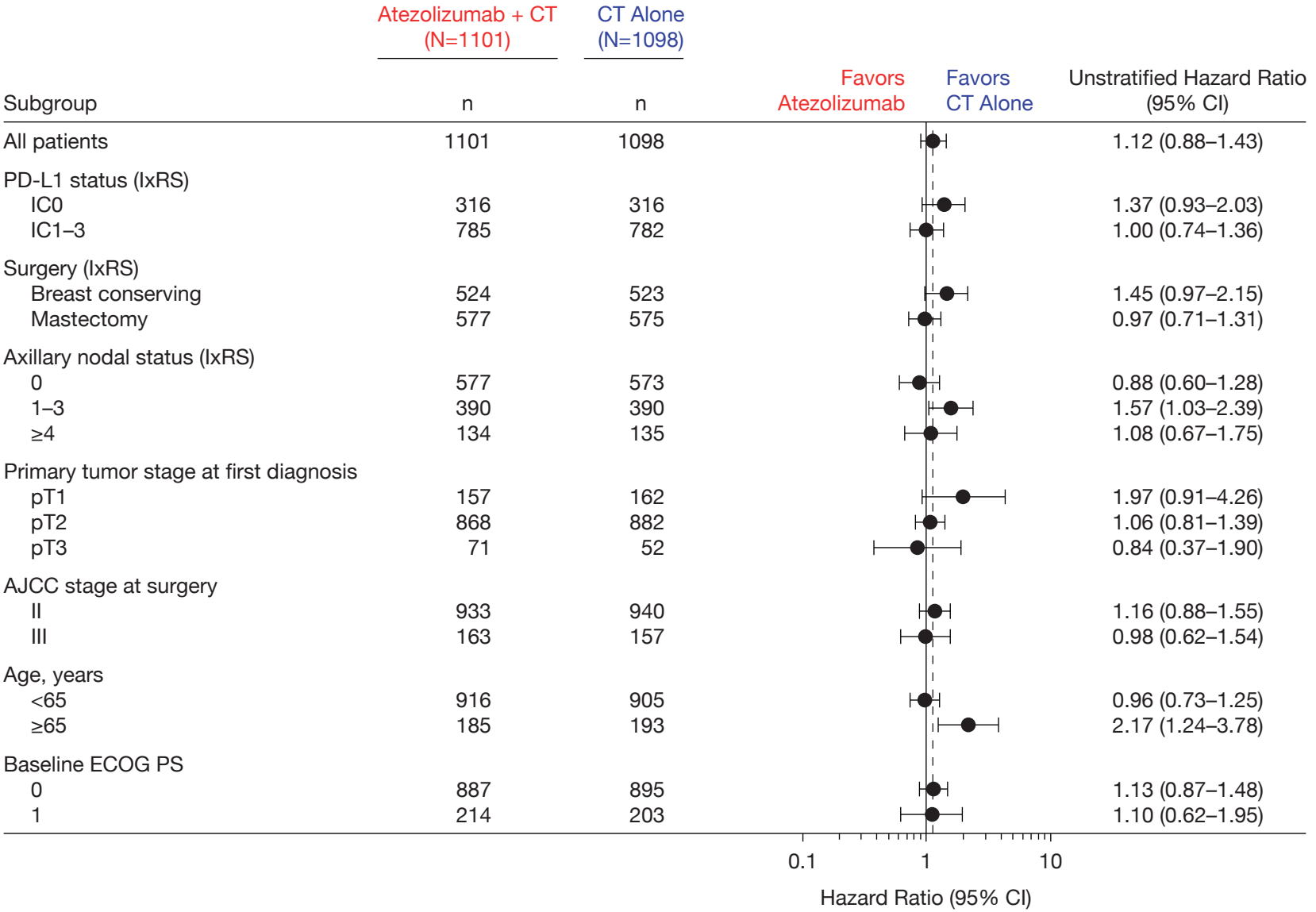



Enrollment
Assessed for eligibility (n=3066)
Excluded (n=867)
Not meeting inclusion criteria (n=591)
Exclusion criterion met (n=70)
Withdrew consent (n=100)
Other (n=106)
Randomized (n=2199)
Allocation
Allocated to atezolizumab + CT (N=1101)
Received allocated intervention (n=1093)
Did not receive allocated intervention (n=8)
Disease relapse (n=1)
Physician decision (n=2)
Patient withdrawal (n=5)
Allocated to CT alone (N=1098)
Received allocated intervention (n=1084)
Did not receive allocated intervention (n=14)
Physician decision (n=3)
Patient withdrawal (n=11)
Follow-up
Discontinued from study (n=1101)
Study terminated by sponsor (n=927)
Died (n=72)
Lost to follow-up (n=26)
Physician decision (n=2)
Patient withdrawal (n=73)
Disease relapse (n=1)
Discontinued from study (n=1098)
Study terminated by sponsor (n=933)
Died (n=58)
Lost to follow-up (n=15)
Physician decision (n=4)
Patient withdrawal (n=88)
Analysi
Analyzed for efficacy (n=1101)
Analyzed for safety (n=1093)
Excluded from safety analysis (n=8)
Not treated (n=8)
Analyzed for efficacy (n=1098)
Analyzed for safety (n=1084)
Excluded from safety analysis (n=14)
Not treated (n=14)



No. at Risk (No. Censored)

Atezolizumab + CT	1101 (0)	1053 (36)	1027 (50)	983 (75)	935 (101)	892 (129)	847 (162)	775 (215)	691 (286)	634 (340)	553 (418)	467 (496)	371 (589)	285 (675)	214 (746)	155 (805)	85 (878)
CT alone	1098 (0)	1041 (45)	1009 (60)	974 (81)	926 (110)	884 (139)	856 (158)	798 (208)	699 (298)	640 (348)	551 (433)	460 (520)	359 (617)	281 (693)	217 (757)	144 (830)	80 (893)


Atezolizumab + CT (N=1101)
CT Alone (N=1098)
Subgroup
n
n
Favors Atezolizumab
Favors CT Alone
Unstratified Hazard Ratio (95% CI)
All patients 1101 1098 1.12 (0.88–1.43)
PD-L1 status (IxRS)
IC0 316 316 1.37 (0.93–2.03)
IC1–3 785 782 1.00 (0.74–1.36)
Surgery (IxRS)
Breast conserving 524 523 1.45 (0.97–2.15)
Mastectomy 577 575 0.97 (0.71–1.31)
Axillary nodal status (IxRS)
0 577 573 0.88 (0.60–1.28)
1–3 390 390 1.57 (1.03–2.39)
≥4 134 135 1.08 (0.67–1.75)
Primary tumor stage at first diagnosis
pT1 157 162 1.97 (0.91–4.26)
pT2 868 882 1.06 (0.81–1.39)
pT3 71 52 0.84 (0.37–1.90)
AJCC stage at surgery
II 933 940 1.16 (0.88–1.55)
III 163 157 0.98 (0.62–1.54)
Age, years
<65 916 905 0.96 (0.73–1.25)
≥65 185 193 2.17 (1.24–3.78)
Baseline ECOG PS
0 887 895 1.13 (0.87–1.48)
1 214 203 1.10 (0.62–1.95)
0.1
1
10
Hazard Ratio (95% CI)