FDA Approval Summary: Atezolizumab Plus Paclitaxel Protein-bound for the Treatment of Patients with Advanced or Metastatic TNBC Whose Tumors Express PD-L1

Preeti Narayan[1], Sakar Wahby[1], Jennifer J. Gao[1], Laleh Amiri-Kordestani[1], Amna Ibrahim[1], Erik Bloomquist[1], Shenghui Tang[1], Yuan Xu[1], Jiang Liu[1], Wentao Fu[1], Pengfei Song[1], Bellinda L. King-Kallimanis[1], Sherry Hou[1], Yutao Gong[1], Shyam Kalavar[3], Soma Ghosh[3], Reena Philip[3], Kirsten B. Goldberg[1,2], Marc R. Theoret[1,2], Gideon M. Blumenthal[1,2], Paul G. Kluetz[1,2], Rajeshwari Sridhara[1], Richard Pazdur[1,2], and Julia A. Beaver[1]

ABSTRACT

On March 8, 2019, the FDA granted accelerated approval to atezolizumab in combination with paclitaxel protein-bound for the treatment of adult patients with unresectable locally advanced or metastatic triple-negative breast cancer (TNBC) whose tumors express PD-L1 [PD-L1 stained tumor-infiltrating immune cells (IC) of any intensity covering ≥1% of the tumor area], as determined by an FDA-approved test. Approval was based on data from IMpassion130, which randomized patients to receive atezolizumab or placebo in combination with paclitaxel protein-bound. Investigator-assessed progression-free survival (PFS) in the intent-to-treat (ITT) and PD-L1–positive populations were coprimary endpoints. After 13-month median follow-up, the estimated median PFS in the PD-L1–positive population was 7.4 months in the atezolizumab arm and 4.8 months in the placebo arm [HR = 0.60; 95% confidence interval (CI), 0.48–0.77]. Overall survival (OS) results were immature with 43% deaths in the ITT population, representing 59% of the OS events required to perform the final OS analysis. Adverse reactions occurring in ≥20% of patients receiving atezolizumab with paclitaxel protein-bound were alopecia, peripheral neuropathies, fatigue, nausea, diarrhea, anemia, constipation, cough, headache, neutropenia, vomiting, and decreased appetite. Accelerated approval was appropriate taking into account the unmet medical need along with the immaturity of the OS results and potential for PFS in the PD-L1–expressing population to predict clinical benefit.

Introduction

In the United States, breast cancer is the most common cancer in women, with more than 260,000 new cases and 40,000 deaths annually (1). Triple-negative breast cancer (TNBC) is characterized immunohistologically by the lack of expression of hormonal receptors [estrogen receptor (ER) and progesterone receptor (PR)], and lack of overexpression and/or amplification of the *HER2/NEU* gene (2). TNBC accounts for approximately 10%–20% of newly diagnosed breast cancer cases (3). Patients with TNBC have a higher risk of both local and distant recurrence, and metastases are more likely to occur in visceral organs and the brain compared with patients with other types of breast cancers (4).

Because of lack of targets, standard of care for patients with locally advanced or metastatic TNBC has traditionally been systemic chemotherapy (e.g., paclitaxel, capecitabine, eribulin, ixabepilone; ref. 5). Despite these treatments, however, most patients have disease progression and the 5-year overall survival is estimated at only 11%. Locally advanced or metastatic TNBC remains a serious disease with unmet medical needs (1). Atezolizumab (Tecentriq, Genentech, Inc.) is an Fc-engineered, humanized, monoclonal IgG1 kappa antibody that directly binds to programmed death-ligand 1 (PD-L1) and blocks its interactions with the PD-1 and B7.1 receptors. Paclitaxel protein-bound is a microtubule inhibitor. Atezolizumab is approved for other indications including bladder cancer and lung cancer. This article summarizes the results and FDA's review leading to the accelerated approval of atezolizumab in combination with paclitaxel protein-bound for the treatment of adult patients with unresectable locally advanced or metastatic TNBC whose tumors express PD-L1 based on trial IMpassion130 (NCT 02425891).

Clinical Pharmacology

Previously, atezolizumab had been approved for administration at 1,200 mg every 3 weeks; in IMpassion130, exposures from administration 840 mg every 2 weeks were consistent with the previously established exposure from every 3-week administration. The treatment-emergent anti-drug antibody (ADA) incidence rate was 13% (57 of 434 patients). This incidence rate is lower than seen in clinical trials of patients with non–small cell lung cancer or urothelial carcinoma who received atezolizumab 1,200 mg every 3 weeks (approximately 30%–48%). This lower ADA incidence rate seen in IMpassion130 may potentially be an underestimation due to a high percentage of patients with C_{trough} above the ADA assay drug tolerance threshold after the first ADA assessment at week 4. Atezolizumab clearance in patients who tested positive for treatment-emergent ADA was 22% higher

[1]Center for Drug Evaluation and Research, U.S. Food and Drug Administration, Silver Spring, Maryland. [2]Oncology Center of Excellence, U.S. Food and Drug Administration, Silver Spring, Maryland. [3]Center for Devices and Radiological Health, U.S. Food and Drug Administration, Silver Spring, Maryland.

Corresponding Author: Preeti Narayan, U.S. Food and Drug Administration, WO22 Room 2331, 10903 New Hampshire Avenue, Silver Spring, MD 20993. Phone 240-402-9523; E-mail: preeti.narayan@fda.hhs.gov

Clin Cancer Res 2020;26:2284–9

doi: 10.1158/1078-0432.CCR-19-3545

compared with clearance in patients who tested negative for treatment emergent ADA. There are insufficient numbers of patients in the PD-L1–positive subgroup with ADA (21 of 178 patients) to determine whether development of ADA alters the efficacy or safety of atezolizumab.

Clinical Trial Design

IMpassion130 was a randomized, placebo-controlled, double-blinded, two-arm trial in patients with locally advanced or metastatic TNBC who had not received prior chemotherapy for metastatic breast cancer (6). Atezolizumab (840 mg) or placebo was administered via intravenous infusions on days 1 and 15 of every 28-day cycle. Paclitaxel protein-bound (100 mg/m^2) was administered via intravenous infusion on days 1, 8, and 15 of every 28-day cycle (3 weeks on/1 week off). The study was initially designed with the coprimary endpoints of progression-free survival (PFS) in the intention-to-treat (ITT) and PD-L1–positive populations. On November 20, 2015, a protocol amendment added overall survival (OS) as a coprimary endpoint and the sample size was increased from 350 to 900 patients to achieve adequate power. The analysis of OS was a hierarchical design with OS in the ITT population needing to reach statistical significance before OS in the PD-L1–positive population could be tested. A total of three analyses of OS were planned (two interim analyses and one final analysis). There were no planned interim analyses for PFS. Secondary endpoints included investigator-assessed objective response rate (ORR), duration of response (DoR), and the patient-reported outcome (PRO) secondary endpoint of time to deterioration in global health status and health-related quality of life. ORR was included in the testing hierarchy. There was no prespecified hypothesis test with type I error allocation for DoR and the PRO endpoints and they are therefore considered exploratory.

Results

Efficacy

Baseline demographics for patients in the ITT and PD-L1 population of IMpassion130 are shown in **Table 1**. A total of 902 patients were randomized between the two arms (451 to atezolizumab + paclitaxel protein-bound, 451 to placebo + paclitaxel protein-bound). Four (0.4%) of the patients were men. Baseline disease characteristics for patients in the ITT and PD-L1 populations are shown in **Table 2**. Almost all patients (99.4%) were triple negative according to local laboratory determination as required as per eligibility criteria. Two patients randomized to the placebo + paclitaxel protein-bound arm and 3 patients randomized to the atezolizumab + paclitaxel protein-bound arm did not have triple-negative disease according to the protocol-defined criteria; these patients remained part of the ITT analysis population. Overall, 41% of enrolled patients had tumors that were PD-L1–positive as tested by the Ventana PD-L1 (SP142) Assay and were balanced between the control and experimental arm. Baseline patient and disease characteristics were well balanced in the ITT and the PD-L1–positive populations and were also similar between the two populations

IMpassion130 demonstrated a statistically significant improvement in PFS in the ITT and PD-L1–positive populations. In the

Table 1. IMpassion130 demographics, ITT and PD-L1 positive population.

Demographic parameters	Atezolizumab + paclitaxel protein-bound (ITT) *N* = 451 (%)	Placebo + paclitaxel protein-bound (ITT) *N* = 451 (%)	Atezolizumab + paclitaxel protein-bound (PD-L1 positive) *N* = 185 (%)	Placebo + paclitaxel protein-bound (PD-L1 positive) *N* = 184 (%)
Sex				
Male	3	1	1	0
Female	448	450	184	184
Age				
Mean (SD)	54.3 (12.3)	55.4 (12.1)	53.7 (12.9)	53.6 (12)
Median	55	56	53	53
Min, max (years)	20–82	26–86	26–82	28–85
Age group				
18–40	63 (14)	51 (11.3)	31 (16.8)	24 (13)
41–64	284 (63)	285 (63.2)	111 (60)	117 (63.6)
≥65	104 (23.1)	115 (25.5)	43 (23.2)	43 (23.4)
Race				
White	308 (68.3)	301 (66.7)	125 (67.6)	129 (70.1)
Asian	85 (18.8)	76 (16.9)	38 (20.5)	28 (15.2)
Black or African American	26 (5.8)	33 (17.3)	9 (4.9)	14 (17.6)
American Indian or Alaska Native	17 (3.8)	23 (5.1)	8 (4.3)	9 (4.9)
Native Hawaiian/Pacific Islander	1 (0.2)	0 (0)	0 (0)	0 (0)
Other[a]	14 (3.1)	18 (4)	5 (2.7)	4 (2.2)
ECOG				
0	256 (56.9)	270 (60)	107 (57.8)	112 (60.9)
1	193 (42.9)	179 (39.8)	77 (41.6)	72 (39.1)
2	1 (0.2)	1 (0.2)	1 (0.5)	0 (0)

Abbreviation: ECOG, Eastern Cooperative Oncology Group.
[a]Other, unknown, multiple.

Table 2. Baseline disease characteristics for IMpassion130, ITT, and PD-L1–positive population.

Demographic parameters	Atezolizumab + paclitaxel protein-bound (ITT) *N* = 451 (%)	Placebo + paclitaxel protein-bound (ITT) *N* = 451 (%)	Atezolizumab + paclitaxel protein-bound (PD-L1 positive) *N* = 185 (%)	Placebo + paclitaxel protein-bound (PD-L1 positive) *N* = 184 (%)
Prior taxane				
Yes	231 (51.2)	230 (51)	96 (51.9)	97 (52.7)
No	220 (48.8)	221 (49)	89 (48.1)	87 (47.3)
Presence of liver metastases				
Yes	126 (27.9)	118 (26.2)	42 (22.7)	41 (22.3)
No	325 (72.1)	333 (73.8)	143 (77.3)	143 (77.7)
PD-L1 Status				
IHC 0	266 (59)	267 (59.2)	0 (0)	0 (0)
IHC 1/2/3	185 (41)	184 (40.8)	185 (100)	184 (100)
Brain metastases				
Yes	30 (6.7)	31 (6.9)	15 (8.1)	11 (6)
No	421 (93.3)	420 (93.1)	170 (91.9)	173 (94)
Nodal only disease				
Yes	33 (7.3)	23 (5.1)	18 (9.7)	13 (7.1)
No	417 (92.7)	426 (94.9)	167 (90.3)	170 (92.9)
Lung metastases				
Yes	226 (50.1)	242 (53.7)	86 (46.5)	98 (53.3)
No	225 (49.9)	209 (46.3)	99 (53.5)	86 (46.7)
Bone metastases				
Yes	145 (32.2)	141 (31.3)	54 (29.2)	49 (26.6)
No	306 (67.8)	310 (68.7)	131 (70.8)	135 (73.4)
Baseline disease status				
Locally advanced unresectable	46 (10.2)	42 (9.3)	23 (12.4)	24 (13.1)
Metastatic	404 (89.8)	408 (90.7)	162 (87.6)	159 (86.9)
Number of sites				
0–3	332 (73.8)	341 (75.9)	149 (80.5)	140 (76.5)
>3	118 (26.2)	108 (24.1)	36 (19.5)	43 (23.5)
Prior anthracycline treatment				
Yes	243 (53.9)	242 (53.7)	109 (58.9)	101 (54.9)
No	208 (46.1)	209 (46.3)	76 (41.1)	83 (45.1)
Prior (neo) adjuvant chemotherapy				
Yes	284 (63)	286 (63.4)	125 (67.6)	117 (63.6)
No	167 (37)	165 (36.6)	60 (32.4)	67 (36.4)

ITT population, a HR of 0.79 [95% confidence interval (CI), 0.68–0.92] was observed with an estimated median PFS difference of 1.5 months (7.0 months vs. 5.5 months). In the PD-L1–positive population, an HR of 0.60 (95% CI, 0.48–0.77) was observed with an estimated median PFS difference of 2.6 months (7.4 months vs. 4.8 months; **Fig. 1**). Other efficacy results are shown in **Table 3**. Adding atezolizumab to paclitaxel protein-bound in the PD-L1–negative population had no effect on PFS; the HR was 0.94 (95% CI, 0.78–1.13) and no median difference was observed (5.6 months vs. 5.6 months).

The OS results at the first interim analysis (389 events in the ITT population) did not cross the interim boundary (HR < 0.759, tested at $\alpha = 0.0065$) for statistical significance, with a HR of 0.84 (95% CI, 0.69–1.02, $P = 0.084$; ref. 6). At this first interim analysis of OS, data were immature with 43% deaths in the ITT population. During the review of the supplemental biologic application, the results of the second interim analysis of OS became available (534 events in the ITT population). At the second interim analysis, the results also did not cross the boundary for statistical significance (HR < 0.818, tested at $\alpha = 0.021$) with a HR of 0.86 (95% CI, 0.72–1.02; $P = 0.077$; ref. 7). Because OS in the ITT population that did not reach statistical significance, due to the hierarchical testing plan the OS results (at the second interim analysis) in the PD-L1–positive population are descriptive and are considered exploratory only (HR = 0.71; 95% CI, 0.54–0.93). Follow-up continues for OS and the final OS is planned when approximately 662 events have occurred. In the PD-L1–positive population, the ORR was 53% for the combination of atezolizumab with paclitaxel protein-bound compared with 33% in the control arm with a difference in duration of response of 3.0 months between arms.

Safety

No new safety signals were identified in IMpassion130 with the addition of atezolizumab to paclitaxel protein-bound (8). In patients who received atezolizumab + paclitaxel protein-bound, the most common treatment-emergent adverse events (TEAE ≥20%) were alopecia (56%), peripheral neuropathies (47%), fatigue (47%), nausea (46%), diarrhea (33%), anemia (28%), constipation (25%), cough (25%), headache (23%), neutropenia (21%), vomiting (20%), and decreased appetite (20%). The events which occurred at a higher incidence (≥5% difference) in the atezolizumab + paclitaxel protein-

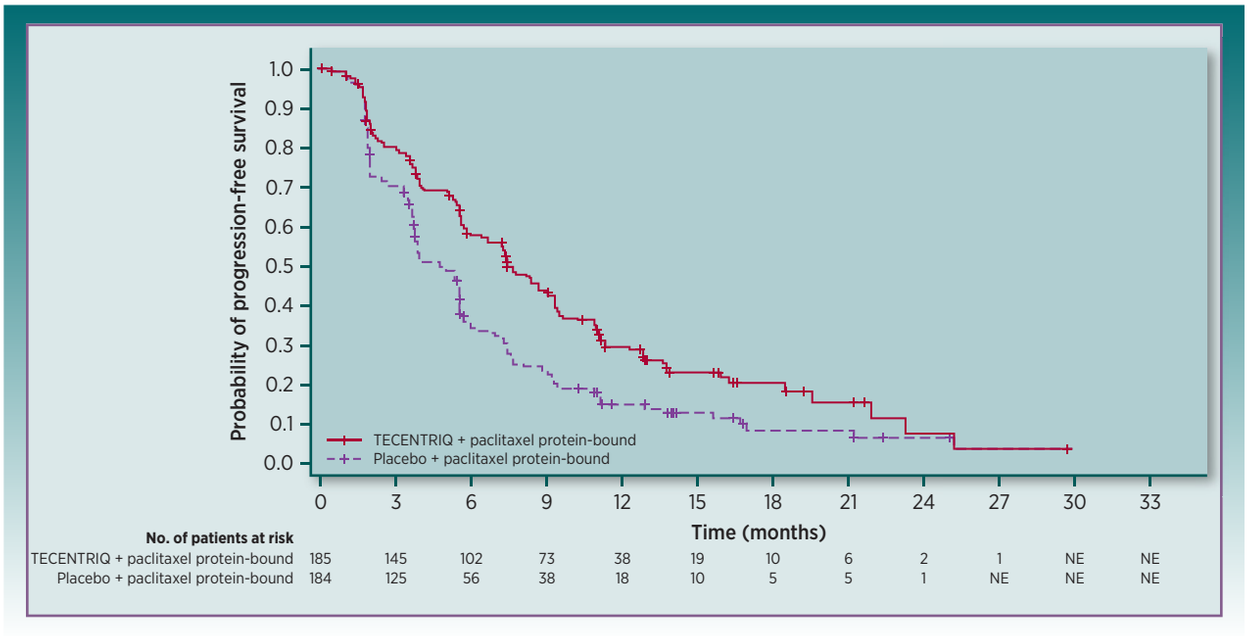

Figure 1.
Kaplan–Meier plot of progression-free survival, PD-L1–positive population.

bound arm compared with the placebo + paclitaxel protein-bound arm were nausea, cough, neutropenia, pyrexia, and hypothyroidism. The most common grade 3–4 adverse reactions occurring in ≥2% were neutropenia (8%), peripheral neuropathies (9%), neutrophil count decreased (4.6%), fatigue (4%), anemia (2.9%), hypokalemia (2.2%), pneumonia (2.2%), and aspartate aminotransferase increased (2.0%).

Table 3. Efficacy results, PD-L1–positive population.

	PD-L1 Expression ≥ 1%[a]	
	Atezolizumab + paclitaxel protein-bound	**Placebo + paclitaxel protein-bound**
Progression-free survival[b,c]	(*n* = 185)	(*n* = 184)
Events (%)	136 (74)	151 (82)
Median, months	7.4 (6.6, 9.2)	4.8 (3.8, 5.5)
Stratified HR (95% CI)[d]	0.60 (0.48–0.77)	
P	<0.0001	
Objective response rate[b,c,e,f]	*n* = 185	*n* = 183
Number of responders (%)	98 (53)	60 (33)
(95% CI)	(45.5–60.3)	(26.0–40.1)
Complete response (%)	17 (9)	1 (<1)
Partial response (%)	81 (44)	59 (32)
Duration of Response[b,c,f]	*n* = 98	*n* = 60
Median (months)	9.2	6.2
(95% CI)	(7.5–11.9)	(5.5–8.8)

Abbreviation: NE, not estimable.
[a]PD-L1 expression in tumor-infiltrating immune cells (IC).
[b]As determined by investigator assessment.
[c]Per Response Evaluation Criteria in Solid Tumors v1.1 (RECIST v1.1).
[d]Stratified by presence of liver metastases, and by prior taxane treatment.
[e]Patients with measurable disease at baseline.
[f]Confirmed responses.

Adverse reactions leading to discontinuation of atezolizumab in the atezolizumab + paclitaxel protein-bound arm occurred in 6% of patients, with peripheral neuropathy (<1%) as the most common adverse reaction leading to discontinuation. Fatal adverse reactions occurred in 1.3% of patients in the atezolizumab + paclitaxel protein-bound arm; these included septic shock, mucosal inflammation, autoimmune hepatitis, aspiration, pneumonia, pulmonary embolism. Serious adverse reactions occurred in 23% of patients. The most frequent serious adverse reactions were pneumonia (2%), urinary tract infection (1%), dyspnea (1%), and pyrexia (1%). Immune-related adverse reactions requiring systemic corticosteroid therapy occurred in 13% of patients and are consistent with the known safety profile of atezolizumab.

Patient-reported Outcomes

Patient-reported outcomes (PRO) were assessed using the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core 30 (QLQ-C30) and other measures. The scales measuring function and global health status/health-related quality of life (GHS/QoL) are transformed onto a 0–100 scoring scale, where higher scores indicate better functioning, whereas for symptom scores, higher scores indicate the symptom is worse (9, 10). In both the ITT and PD-L1–positive populations, completion rates of the EORTC QLQ-C30 at baseline was similar for both treatment arms (>90%). Completion rates for both arms were above 80% through cycle 7 when ≥50% of the ITT and PD-L1–positive populations were still on treatment. PRO endpoints were not prespecified with type I error allocation. Exploratory objectives were to evaluate PRO measures of GHS/QoL, function and disease/treatment-related symptoms associated with both treatment arms. Over the first 12 months of therapy, differences between the arms with respect to GHS/QoL and physical functioning were small. For

Table 4. FDA risk–benefit analysis.

Dimensions	Evidence and uncertainties	Conclusions and reasons
Analysis of condition	• Locally advanced or metastatic TNBC has a poor prognosis and is a serious and life-threatening condition. • Approximately 40,000 women die from breast cancer each year.	Locally advanced and metastatic TNBC is a serious and life-threatening condition with significant unmet medical need.
Current treatment options	• There are no FDA-approved treatment options for patients with TNBC with PD-L1 expression ≥1%.	All currently available treatment options are palliative and have significant adverse reactions or intolerance.
Benefit	• IMpassion130 enrolled 902 patients with unresectable locally advanced or metastatic TNBC that had not received prior chemotherapy for metastatic disease. • In patients with PD-L1 expression ≥1%, the stratified HR for PFS was 0.60 (95% CI, 0.48–0.77; $P < 0.0001$) in favor of the atezolizumab and paclitaxel protein-bound arm. The estimated median PFS was 7.4 months (6.6–9.2 months) in the atezolizumab and paclitaxel protein-bound arm compared with 4.8 months (3.8–5.5 months) in the placebo and paclitaxel protein-bound arm. • ORR in patients with PD-L1 expression ≥1% with confirmed responses was 53% compared with 33%, in favor of the atezolizumab and paclitaxel protein-bound arm.	In IMpassion130, atezolizumab with paclitaxel protein-bound in patients with TNBC with PD-L1 expression ≥1% showed results in PFS reasonably likely to demonstrate clinical benefit. A companion diagnostic is essential for safe and effective use. Overall survival data were immature.
Risk and risk management	• No new safety signals were identified.	The profile of adverse reactions is similar to that observed in other PD-(L)1–targeted products and consistent with the known safety profile of atezolizumab and paclitaxel protein-bound. The safe use of atezolizumab with paclitaxel protein-bound can be managed through accurate labeling. No REMS is indicated.

Abbreviation: REMS, risk evaluation and mitigation strategy.

example, at baseline for patients in the atezolizumab + paclitaxel protein-bound arm, mean physical function was 82.8, the largest decrease over the first 12 months was at cycle 5, where the mean dropped to 76.8. In the placebo arm, baseline mean was 79.4 and the largest decrease was to 75.3 at cycle 11. In both the ITT and PD-L1–positive populations, there did not appear to be large difference for treatment-related symptoms (fatigue, diarrhea, nausea, and vomiting) between the treatment arms.

Regulatory Insights

This is the first FDA approval for patients with locally advanced or metastatic TNBC, and the first FDA approval for immunotherapy in breast cancer (11). IMpassion130 demonstrated a statistically significant improvement in PFS with the addition of atezolizumab to paclitaxel protein-bound in both the ITT and PD-L1–positive population. The safety profile was consistent with the known safety profile of atezolizumab and paclitaxel protein-bound and was acceptable for the intended population. The magnitude of benefit was greater in the PD-L1–positive population and patients with PD-L1–negative tumors did not appear to derive clinical benefit. Therefore, the benefit-risk profile was not deemed appropriate for treatment of patients without PD-L1 expression, and the Ventana PD-L1 (SP142) Assay was contemporaneously approved as a companion diagnostic device essential for the safe and effective use of atezolizumab to select for patients with tumors expressing PD-L1. While there are multiple biomarkers across disease types that have been used to evaluate and potentially demonstrate differential benefit of immunotherapy, PD-L1 was the studied biomarker in this trial and therefore the companion diagnostic biomarker reflected the studied population and results.

Although the IMpassion130 study was conducted in patients with previously untreated locally advanced or metastatic TNBC, given the availability of other standard-of-care options for first-line treatment, potential for benefit regardless of line of therapy, the seriousness of the condition, the acceptable safety profile, and need for additional effective therapies in patients with TNBC, the indication was not restricted to the first-line setting. This will allow for a discussion of benefit/risk between the provider and patient and will also allow those patients who were not newly diagnosed with metastatic disease at the time of approval to discuss the potential to receive this new treatment option later in their treatment course with the caveat that the exact magnitude of benefit in later lines of therapy is not known. The FDA risk–benefit analysis is shown in **Table 4**.

While PFS was statistically significant in IMpassion130, the median improvement in PFS in the PD-L1 subgroup was modest for an add-on design trial, indicating this improvement may not represent direct clinical benefit. However, the PFS result for the PD-L1 population appeared reasonably likely to predict clinical benefit and thus in the context life-threatening breast cancer was appropriate for accelerated approval. Because of the prespecified statistical analysis plan, OS in the PD-L1 population could not be tested, with appropriate type I error control, Because OS in the ITT population did not reach statistical significance. Results from an ongoing multicenter, randomized, double-blind, placebo-controlled study of atezolizumab or placebo with paclitaxel in patients with previously untreated, inoperable, locally advanced, or metastatic TNBC (IMpassion131, NCT03125902) may provide confirmatory evidence from PFS with supportive OS information to verify the clinical benefit in the same patient population. Alternatively, final OS results from IMpassion130 may also provide confirmatory evidence to verify the clinical benefit.

Conclusions

In summary, atezolizumab plus paclitaxel protein-bound for the treatment of patients with locally advanced or metastatic TNBC whose tumors express PD-L1 (PD-L1 stained tumor-infiltrating IC of any intensity covering ≥ 1% of the tumor area), demonstrates a favorable benefit-risk profile with results reasonably likely to demonstrate clinical benefit. No new safety signals were observed, and the safety profile is acceptable for patients with metastatic TNBC. Because statistical significance was not reached for OS in the ITT population, we cannot adequately determine whether any observed difference in OS in the PD-L1–positive population is due to chance. With the residual uncertainty of the benefit of the addition of atezolizumab to paclitaxel-protein bound, the results from IMpassion130 supported an accelerated approval. Continued approval for this indication may be contingent upon verification of clinical benefit from other ongoing clinical trials.

Disclosure of Potential Conflicts of Interest

J. J. Gao is a paid consultant for Worldcare, Inc. No potential conflicts of interest were disclosed by the other authors.

Disclaimer

The Editor handling the peer review and decision-making process for this article has no relevant employment associations to disclose.

Authors' Contributions

Conception and design: P. Narayan, J.J. Gao, P.G. Kluetz, R. Pazdur, J.A. Beaver
Development of methodology: P. Narayan, J.J. Gao, R. Pazdur, J.A. Beaver
Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): S. Wahby, J.J. Gao, B.L. King-Kallimanis
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): P. Narayan, S. Wahby, J.J. Gao, L. Amiri-Kordestani, S. Tang, Y. Xu, J. Liu, W. Fu, P. Song, Y. Gong, S. Ghosh, R. Philip, G.M. Blumenthal, P.G. Kluetz, R. Sridhara, R. Pazdur, J.A. Beaver
Writing, review, and/or revision of the manuscript: P. Narayan, S. Wahby, J.J. Gao, L. Amiri-Kordestani, E. Bloomquist, S. Tang, Y. Xu, J. Liu, W. Fu, P. Song, B.L. King-Kallimanis, S. Kalavar, S. Ghosh, R. Philip, K.B. Goldberg, M.R. Theoret, G.M. Blumenthal, P.G. Kluetz, R. Sridhara, R. Pazdur, J.A. Beaver
Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): J.J. Gao, A. Ibrahim, R. Philip, K.B. Goldberg, R. Pazdur
Study supervision: J.J. Gao, R. Pazdur, J.A. Beaver
Other (regulatory project management): S. Hou

Received October 28, 2019; revised December 16, 2019; accepted January 27, 2020; published first January 30, 2020.

References

1. National Cancer Institute. Surveillance, Epidemiology and End Results Program (SEER). Female breast cancer; 2019. Available from: https://seer.cancer.gov/statfacts/html/breast.html.
2. Dent R, Trudeau M, Pritchard KI, Hanna WM, Kahn HK, Sawka CA, et al. Triple-negative breast cancer: clinical features and patterns of recurrence. Clin Cancer Res 2007;13:4429–34.
3. Foulkes WD, Smith IE, Reis-Filho JS. Triple-negative breast cancer. N Engl J Med 2010;363:1938–48.
4. Carey LA, Perou CM, Livasy CA, Dressler LG, Cowan D, Conway K, et al. Race, breast cancer subtypes, and survival in the Carolina Breast Cancer Study. JAMA 2006;295:2492–502.
5. National Comprehensive Cancer Network (NCCN) Guidelines. Breast cancer [about 4 screens]; 2019. Available from: https://www.nccn.org/professionals/physician_gls/default.aspx.
6. Schmid P, Adams S, Rugo HS, Schneeweiss A, Barrios CH, Iwata H, et al. Atezolizumab and nab-paclitaxel in advanced triple negative breast cancer. N Engl J Med 2018;379:2108–21.
7. Schmid P, Rugo HS, Adams S, Schneeweiss A, Barrios CH, Iwata H, et al. Atezolizumab plus nab-paclitaxel as first-line treatment for unresectable, locally advanced or metastatic triple-negative breast cancer (IMpassion130): updated efficacy results from a randomized, double-blind, placebo-controlled, phase 3 trial. Lancet Oncol 2020;21:44–59.
8. Drugs@FDA: FDA-Approved Drugs. TECENTRIQ (atezolizumab), supplement 18 label and letter 3/8/19 [about 4 screens]; 2019. Available from: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=761034.
9. Bergman B, Aaronson NK, Ahmedzai S, Kaasa S, Sullivan M. The EORTC QLQ-LC13: a modular supplement to the EORTC Core Quality of Life Questionnaire (QLQ-C30) for use in lung cancer clinical trials. EORTC Study Group on Quality of Life. Eur J Cancer 1994;30A:635–42.
10. EuroQol Group. EuroQol -a new facility for the measurement of health-related quality of life. Health Policy 1990;16:199–208.
11. U.S. Food and Drug Administration. FDA drug approvals and databases: FDA approves atezolizumab for PD-L1 positive unresectable locally advanced or metastatic triple-negative breast cancer [about 3 screens]; 2019. Available from: https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-atezolizumab-pd-l1-positive-unresectable-locally-advanced- or-metastatic-triple-negative.