Humanistic Burden in Metastatic Triple-Negative Breast Cancer: A Systematic Literature Review

Poster # PCR258

Yuanhui Zhang[1], Iwona Pustulka[2], Anandaroop Dasgupta[1], Marissa Betts[3], Ryan Thaliffdeen[1], Sonya Egodage[4], Henry Ogden[5], Manali Ajay Bhave[6]

[1]Gilead Sciences, Inc., Foster City, CA, USA; [2]Evidera Inc., Poland Domaniewska, Warsaw, Poland; [3]Evidera Inc., Waltham, MA, USA; [4]Evidera Ltd., Bethesda, MD, USA; [5]Evidera Ltd., London, UK; [6]Winship Cancer Institute, Emory University, Atlanta, GA, USA

Conclusions

- In patients with metastatic triple-negative breast cancer (mTNBC), health-related quality of life (HRQOL) generally decreased as patients progressed to later lines of therapy
- In the second-line (2L) or later setting, sacituzumab govitecan (SG) showed statistically significant improvement in HRQOL vs chemotherapy
- In the first-line (1L) setting, immunotherapy showed mixed results; pembrolizumab demonstrated HRQOL improvement in programmed death ligand 1 (PD-L1)-positive patients vs chemotherapy
- In observational studies of patients with mTNBC, gemcitabine + capecitabine showed significant improvement in HRQOL vs docetaxel + capecitabine, and capecitabine + cytokine-induced killer (CIK) cell therapy significantly improved HRQOL vs capecitabine alone, although sample size was small
- This systematic literature review (SLR) underscores the unmet need for new therapies that can enable improvements or extend maintenance of HRQOL for patients with mTNBC while lengthening survival, especially in the first line setting

Plain Language Summary

- Recent advancements in breast cancer treatment have resulted in people with metastatic triple-negative breast cancer (mTNBC) living longer. However, it is not clear if longer survival is accompanied by improved quality of life (a measure of a person's sense of well-being and their ability to do daily activities)
- People with mTNBC had improved quality of life if they received a drug called sacituzumab govitecan as second-line or later treatment
- People with mTNBC whose tumors expressed a protein called PD-L1 had improved quality of life from first-line treatment when they received a drug called pembrolizumab, which targets PD-L1
- While current treatments can improve quality of life in people with mTNBC, there is a need for new drugs that further improve or maintain quality of life while also extending survival, especially in the first line setting of treatment

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Correspondence: Yuanhui Zhang, Yuanhui.Zhang33@gilead.com

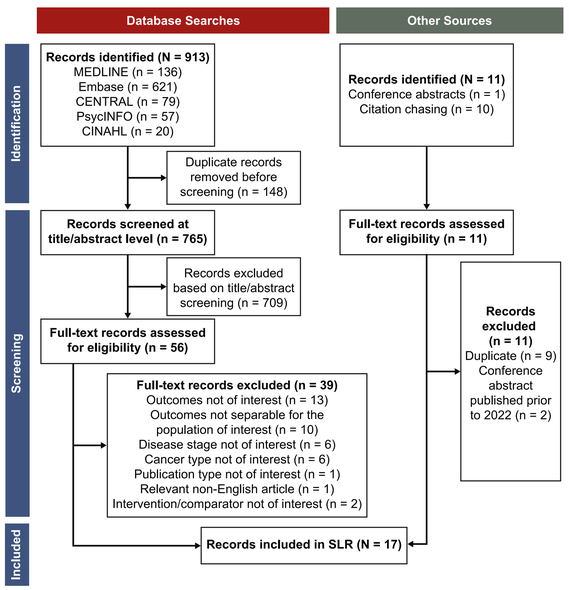
Introduction

- Breast cancer is the most common cancer in women,[1] and triple-negative breast cancer (TNBC) accounts for approximately 11% of breast cancer cases[2,3]
- Prognosis for mTBNC remains poor, with 5-year overall survival rates of 7% to 14% across countries,[3-5] and a substantial reduction in HRQOL[6-7]
- Recent advances in mTNBC treatment, such as the introduction of PD-(L)1 inhibitors (targeting programmed cell death protein-1 [PD-1] or PD-L1), have improved clinical outcomes in PD-L1 positive patients[8]; however, these advances have not necessarily been accompanied by significant improvements in HRQOL
- We present an SLR of HRQOL and utility/disutility values in patients with mTNBC, divided by PD-L1 status, with the goal of better understanding how recent advances in treatment options may affect HRQOL

Methods

- An SLR was conducted according to Cochrane methodologies; searches were conducted across Embase, MEDLINE and MEDLINE In-Process, APA PsycINFO, Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews (CDSR), and Cumulative Index to Nursing and Allied Health Literature (CINAHL) from the date of each database inception to June 2024
- Gray literature searches were also conducted to identify relevant information in conference abstracts, clinical trial registries, health technology assessment submissions, and product labels; conference abstracts prior to 2022 were excluded
- English language studies of mTNBC or mixed-stage TNBC were included; items that included non-TNBC cancer types were only included if results were available for the TNBC subgroup or if the proportion of patients with TNBC was ≥ 80%
- A total of 924 records were identified, and after screening, 17 of these records were included in the analysis (**Figure 1**)

Figure 1. Literature Search Diagram



CENTRAL, Cochrane Central Register of Controlled Trials; CINAHL, Cumulative Index to Nursing and Allied Health Literature; SLR, systematic literature review.

Results

- Among the 17 records included, there were 13 studies (7 clinical and 6 observational studies)
- Characteristics of these studies are summarized in (**Table 1**)

Results

Table 1. Study Characteristics

Study	Population	Treatment	PD-L1 Status of Patients	N
Clinical Studies				
ASCENT[9]	Refractory/relapsed mTNBC (3L+)	SG	AC	236
		TPC		183
IMpassion130[10]	Unresectable locally advanced or mTNBC (1L)	Atezo + NP	AC	451
			PD-L1+[a]	185
		Pbo + NP	AC	451
			PD-L1+[a]	184
KEYLYNK-009[11]	Locally advanced inoperable or mTNBC (1L)	Pembro + Ola	AC	135
		Pembro + Chemo		136
KEYNOTE-119[12]	mTNBC (2L or 3L)	Pembro	AC	312
			PD-L1+[b]	96
		Chemo	AC	310
			PD-L1+[b]	98
KEYNOTE-355[13]	mTNBC (1L)	Pembro + Chemo	AC	566
			PD-L1+[b]	220
		Pbo + Chemo	AC	281
			PD-L1+[b]	103
OlympiAD[14]	*BRCA*-mutated, HER2– mBC (TNBC subgroup) (≤ 3L)	Ola	AC	102
		Chemo	AC	48
TBCRC 018[15]	mTNBC (Any line)	Inip + Irin	AC	37
Observational Studies				
Chen 2021[16]	Stage IV TNBC (2L or 3L)	Cape metronomic Chemo + autologous CIK cell IO	AC	55
		Metronomic Chemo		55
Ndirangu 2024[17]	Stage III and mTNBC (1L)	N/A	AC	120
	Stage III and mTNBC (2L)	N/A	AC	97
	Stage III and mTNBC (3L+)	N/A	AC	46
Popalis 2023[18]	Early stage and mTNBC	N/A	AC	209
Vadaparampil 2017[19]	Black women aged > 50 years, early stage and mTNBC	N/A	AC	85
Wang 2024[20]	Advanced TNBC	Gem + Cape	AC	42
		Doce + Cape	AC	38
Yamaguchi 2024[21]	mTNBC	Chemo, SG, tertiary therapy	AC	56

[a]PD-L1 positivity criteria: ≥ 1% IC+. [b]PD-L1 positivity criteria: CPS ≥ 10 or CPS ≥ 1.
1L, first line; 2L, second line; 3L+, third-line or later; AC, all-comers; Atezo, atezolizumab; Cape, capecitabine; Chemo, chemotherapy; CIK, cytokine-induced killer; CPS, combined positive score; Doce, docetaxel; Gem, gemcitabine; HER2, human epidermal growth factor receptor 2; Inip, iniparib; IO, immunotherapy; Irin, irinotecan; mBC, breast cancer; mTNBC, metastatic triple-negative breast cancer; N/A, not applicable; NP, Nab-paclitaxel; Ola, olaparib; Pbo, placebo; Pembro, pembrolizumab; PD-(L)1, programmed death (ligand)-1; Pt, platinum; SG, sacituzumab govitecan; TNBC, triple-negative breast cancer; TPC, treatment of physician's choice.

Results From Clinical Studies

- Of 3 studies that analyzed PD-L1–positive patients, only KEYNOTE-119 demonstrated significant differences in HRQOL between treatment arms (pembrolizumab vs chemotherapy) (**Table 2**)

Table 2. HRQOL From Clinical Studies in PD-L1 Positive Patients

Study	Treatment	Tool	PD-L1 Status of Patients: Statistically Significant	PD-L1 Status of Patients: Nonsignificant
Clinical Studies				
IMpassion130[10]	Atezo + NP	EORTC QLQ-C30	• None	• TTD, GHS/QOL score, physical functioning score, role functioning score, cognitive functioning score
	Pbo + NP			
KEYNOTE-119[12]	Pembro	EORTC QLQ-C30	• CPS ≥ 1: Physical functioning diff in % improved –12.12 (95% CI –19.90 to –4.45), *P* < .05	CPS ≥ 1: • LSM diff, GHS/QOL • GHS/QOL, nausea/ vomiting, diarrhea, systemic therapy side effects diff in % improved CPS ≥ 10: • LSM diff, GHS/QOL
	Chemo			
	Pembro	EQ-5D-3L	• None	CPS ≥ 1: • LSM diff, VAS
	Chemo			
KEYNOTE-355[13]	Pembro + Chemo	EORTC QLQ-C30	• None	• LSM diff, GHS/QOL, emotional functioning, physical functioning
	Pbo + Chemo			
	Pembro + Chemo	EQ-5D-3L	• None	• LSM diff, VAS
	Pbo + Chemo			

Atezo, atezolizumab; Chemo, chemotherapy; CPS, combined positive score; Diff, difference; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality-of-Life Questionnaire-Core 30; EQ-5D-3L, EuroQol-5 Dimensions-3 Levels; GHS, global health score; HRQOL, health-related quality of life; LSM, least square mean; NP, Nab-paclitaxel; Pbo, placebo; PD-(L)1, programmed death (ligand)-1; Pembro, pembrolizumab; QOL, quality of life; TTD, time to deterioration; VAS, visual analog scale.

- SG and pembrolizumab demonstrated significant improvements in HRQOL compared to chemotherapy comparators (**Table 3**)

Table 3. HRQOL From All-Comers Clinical Studies

Study	Treatment	Tool	HRQOL Measure Differences: Statistically Significant	HRQOL Measure Differences: Nonsignificant
ASCENT[9,22]	SG	EORTC QLQ-C30	• CFB, summary score at C6: LSM diff 2.48 (95% CI, 0.14-4.81), *P* < .05 • TTI, summary score: HR 1.562 (95% CI, 1.008-2.423), *P* = .0462 • CFB, GHS/QOL score at C6 ◦ Total pop: LSM diff 4.08 (95% CI, 0.82-7.35), *P* < .05 ◦ NA pop: LSM diff 5.492 (95% CI, 1.488-9.497), *P* = .007	• Summary score, BSL • GHS/QOL score, BSL • TTD, GHS/QOL score (total pop, EU pop, US pop) • TTI, GHS/QOL score • CFB, GHS/QOL score (non-NA pop, PR/CR pop, SD/PD/NE pop)
	TPC			
IMpassion130[10]	Atezo + NP	EORTC QLQ-C30	• None	• TTD, GHS/QOL score, physical functioning score, role functioning score, cognitive functioning score
	Pbo + NP			
KEYLYNK-009[11]	Pembro + Ola	EORTC QLQ-C30	• None	• LSM diff, GHS/QOL, physical functioning, emotional functioning, systemic therapy side effects
	Pembro + Chemo			
	Pembro + Ola	EQ-5D-5L	• None	• LSM diff, VAS
	Pembro + Chemo			
KEYNOTE-119[12]	Pembro	EORTC QLQ-C30	• Physical functioning diff in % improved –9.44 (95% CI –15.65 to –3.32), *P* < .05	• GHS/QOL LSM diff • Diff in % improved, GHS/QOL, nausea/ vomiting, diarrhea, systemic therapy side effect
	Chemo			
	Pembro	EQ-5D-3L	• LSM diff, VAS at 6 weeks –3.28 (95% CI –6.33 to –0.24), *P* < .05	• None
	Chemo			
KEYNOTE-355[13]	Pembro + Chemo	EORTC QLQ-C30	• None	• LSM diff, GHS/QOL, emotional functioning, physical functioning
	Pbo + Chemo			
	Pembro + Chemo	EQ-5D-3L	• None	• LSM diff, VAS
OlympiAD[14]	Ola	EORTC QLQ-C30	• None	• CFB in GHS/QOL
	Chemo			
TBCRC 018[15]	Inip + Irin	FACT-G	• CFB, physical well-being 3.1 (NR), *P* < .01	• CFB, emotional well-being, social/family well-being, functional well-being, breast cancer subscale, brain cancer subscale

Atezo, atezolizumab; BSL, baseline; C6, cycle 6; CFB, change from baseline; Chemo, chemotherapy; CR, complete response; diff, difference; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality-of-Life Questionnaire-Core 30; EQ-5D-3L, EuroQol-5 Dimensions-3 Levels; EQ-5D-5L, EuroQol-5 Dimensions-5 Levels; EU, Europe; FACT-G, Functional Assessment of Cancer Therapy- General; GHS, global health score; HRQOL, health-related quality of life; Inip, iniparib; Irin, irinotecan; LSM, least square mean; NA, North America; NE, not evaluable; NP, Nab-paclitaxel; NR, not reported; Ola, olaparib; Pbo, placebo; PD, progressive disease; Pembro, pembrolizumab; Pop, population; PR, partial response; QOL, quality of life; SD, stable disease; SG, sacituzumab govitecan; TPC, treatment of physician's choice; TTD, time to deterioration; TTI, time to improvement; VAS, visual analog scale.

Results From Observational Studies

- None of the observational studies reported results from patients with PD-L1–positive tumors specifically
- Two studies compared alternative chemotherapy regimens (capecitabine + CIK cell therapy vs capecitabine; gemcitabine + capecitabine vs docetaxel + capecitabine) on functional scales using different instruments (ie, Functional Assessment of Cancer Therapy-Breast Symptom Index scores and European Organization for Research and Treatment of Cancer-Quality of Life Questionnaire Core 30 [EORTC QLQ-C30])[16,20]
- An observational study showed that both HRQOL (measured by EORTC QLQ-C30 global health status/quality of life domain) and patients' satisfaction on treatment (measured by Cancer Therapy Satisfaction Questionnaire) decreased from 1L to 2L to 3L+[17]

Utility/Disutility Values

- Utility values (scores that express value and quantity of life spent in a given health state and allow calculation of quality-adjusted life years) appeared to be higher in preprogression vs postprogression (EORTC QLQ-C30, UK tariff; 0.710 vs 0.653 with SG and 0.626 vs 0.569 with TPC),[24] and in 1L vs 2L (EQ-5D-5L; 0.77 vs 0.71)[17]
- Yamaguchi 2024 reported disutility values (lead time-trade off; Japanese tariff) for nausea/vomiting (–0.801) and neutropenia (–0.007)[21]