



COMPENDIA TRANSPARENCY TRACKING FORM

DATE: 10/5/2020

PACKET: 2030

DRUG: Pembrolizumab

USE: Triple-negative breast cancer; Early, neoadjuvant, in combination with standard chemotherapy

COMPENDIA TRANSPARENCY REQUIREMENTS	
1	Provide criteria used to evaluate/prioritize the request (therapy)
2	Disclose evidentiary materials reviewed or considered
3	Provide names of individuals who have substantively participated in the review or disposition of the request and disclose their potential direct or indirect conflicts of interest
4	Provide meeting minutes and records of votes for disposition of the request (therapy)

EVALUATION/PRIORITIZATION CRITERIA: C, L, R, S \*to meet requirement 1

CODE	EVALUATION/PRIORITIZATION CRITERIA
A	Treatment represents an established standard of care or significant <b>advance</b> over current therapies
C	<b>Cancer</b> or cancer-related condition
E	Quantity and robustness of <b>evidence</b> for use support consideration
L	<b>Limited</b> alternative therapies exist for condition of interest
P	<b>Pediatric</b> condition
R	<b>Rare</b> disease
S	<b>Serious</b> , life-threatening condition

Note: a combination of codes may be applied to fully reflect points of consideration [eg, therapy may represent an advance in the treatment of a life-threatening condition with limited treatment alternatives (ASL)]



**EVIDENCE CONSIDERED:**

\*to meet requirements 2 and 4

CITATION	STUDY-SPECIFIC COMMENTS	LITERATURE CODE
Schmid, P, Cortes, J, Pusztai, L, et al: Pembrolizumab for early triple-negative breast cancer. N Engl J Med Feb 27, 2020; Vol 382, Issue 9; pp. 810-821.	This was a double-blind, placebo-controlled, randomized Phase III trial that assessed neoadjuvant and adjuvant pembrolizumab in patients with early triple-negative breast cancer. The risk of potential bias associated with randomization, allocation concealment, performance, detection, attrition, and reporting were all deemed low. No other sources of bias were found.	S
Cortes, J, Cescon, DW, Rugo, HS, et al: KEYNOTE-355: Randomized, double-blind, phase III study of pembrolizumab + chemotherapy versus placebo + chemotherapy for previously untreated locally recurrent inoperable or metastatic triple-negative breast cancer. J Clin Oncol 2020; Vol 38, Issue 15 Suppl; p. 1000.		4
Cortes, J, Lipatov, O, Im, SA, et al: KEYNOTE-119: phase III study of pembrolizumab (pembro) versus single-agent chemotherapy (chemo) for metastatic triple negative breast cancer (mTNBC). Ann Oncol Oct 01, 2019; Vol 30 Suppl 5, pp. v859-v860.		4
Adams, S, Schmid, P, Rugo, HS, et al: Pembrolizumab monotherapy for previously treated metastatic triple-negative breast cancer: cohort A of the phase II KEYNOTE-086 study. Ann Oncol Mar 01, 2019; Vol 30, Issue 3; pp. 397-404.		3



<p>Adams, S, Loi, S, Toppmeyer, D, et al: Pembrolizumab monotherapy for previously untreated, PD-L1-positive, metastatic triple-negative breast cancer: cohort B of the phase II KEYNOTE-086 study. Ann Oncol Mar 01, 2019; Vol 30, Issue 3; pp. 405-411.</p>		3
<p>Schmid, P, Salgado, R, Park, YH, et al: Pembrolizumab plus chemotherapy as neoadjuvant treatment of high-risk, early-stage triple-negative breast cancer: results from the phase 1b open-label, multicohort KEYNOTE-173 study. Ann Oncol May 2020; Vol 31, Issue 5; pp. 569-581.</p>		3
<p>Vinayak, S, Tolaney, SM, Schwartzberg, L, et al: Open-label clinical trial of niraparib combined with pembrolizumab for treatment of advanced or metastatic triple-negative breast cancer. JAMA Oncol Jun 13, 2019; Vol 5, Issue 8; pp. 1132-1140.</p>		3
<p>Nanda, R, Chow, LQM, Dees, EC, et al: Pembrolizumab in patients with advanced triple-negative breast cancer: phase 1b KEYNOTE-012 study. J Clin Oncol Jul 20, 2016; Vol 34, Issue 21; pp. 2460-2467.</p>		3



Page, DB, Chun, B, Pucilowska, J, et al: Pembrolizumab (pembro) with paclitaxel (taxol) or capecitabine (cape) as early treatment of metastatic triple-negative breast cancer (mTNBC). J Clin Oncol May 01, 2019; Vol 37 Suppl 15, p. 1015.		3
Ho, AY, Barker, CA, Arnold, BB, et al: A phase 2 clinical trial assessing the efficacy and safety of pembrolizumab and radiotherapy in patients with metastatic triple-negative breast cancer. Cancer Feb 15, 2020; Vol 126, Issue 4; pp. 850-860.		3
Shah, AN, Flaum, L, Helenowski, I, et al: Phase II study of pembrolizumab and capecitabine for triple negative and hormone receptor-positive, HER2-negative endocrine-refractory metastatic breast cancer. J Immunother Cancer Feb 2020; Vol 8, Issue 1; p. e000173.		3
Simmons CE, Brezden-Masley C, McCarthy J, et al. Positive progress: current and evolving role of immune checkpoint inhibitors in metastatic triple-negative breast cancer. Therapeutic Advances in Medical Oncology, vol. 12, First Published March 20, 2020.		4

Literature evaluation codes: S = Literature selected; 1 = Literature rejected = Topic not suitable for scope of content; 2 = Literature rejected = Does not add clinically significant new information; 3 = Literature rejected = Methodology flawed/Methodology limited and unacceptable; 4 = Other (review article, letter, commentary, or editorial)



**CONTRIBUTORS:**

\*to meet requirement 3

PACKET PREPARATION	DISCLOSURES	EXPERT REVIEW	DISCLOSURES
Megan Smith	None		
Stacy LaClaire, PharmD	None		
Catherine Sabatos, PharmD	None		
		John D Roberts	None
		Jeffrey Klein	None
		Richard LoCicero	Incyte Corporation  Local PI for REVEAL. Study is a multicenter, non-interventional, non-randomized, prospective, observational study in an adult population for patients who have been diagnosed with clinically overt PV and are being followed in either community or academic medical centers in the US who will be enrolled over a 12-month period and observed for 36 months.

**ASSIGNMENT OF RATINGS:**

\*to meet requirement 4

	EFFICACY	STRENGTH OF RECOMMENDATION	COMMENTS	STRENGTH OF EVIDENCE
<b>IBM MICROMEDEX</b>	Evidence is Inconclusive	Class III: Not Recommended		B
Jeffrey Klein	Evidence Favors Efficacy	Class IIa: Recommended, in Most Cases	The addition of Pembrolizumab to chemotherapy demonstrated a higher patient complete response than chemotherapy and placebo fo triple neagative breast cancer patients. The adverse effect profile, especially of the serious type has to potential to limit pembrolizumab use though.	



John Roberts	Evidence is Inconclusive	Class III: Not Recommended	Early results from a single randomized, placebo controlled trial indicate an increase in complete pathological response rate and event free survival in patients with early stage, triple-negative breast cancer receiving neoadjuvant and adjuvant pembrolizumab in combination with standard chemotherapy. Additional toxicity was manageable. In a similar time frame, a similar study of adjuvant capecitabine showed a survival benefit. Although results with pembrolizumab are promising, it would be premature to recommend it in the absence of favorable survival data, which presumably will be forthcoming.	
Richard LoCicero	Evidence is Inconclusive	Class III: Not Recommended	The addition of pembrolizumab to chemotherapy for the neoadjuvant treatment of stage II and III triple negative breast cancer was associated with an improvement in pathologic complete response (pCR) rate in a single phase III trial. No unexpected toxicity was observed. While pCR rate may be associated with improvements in other outcomes (such as event-free survival [EFS]), the data in this trial was not mature enough to establish EFS benefit (a primary end point in this trial).	