IBM Watson Health™

COMPENDIA TRANSPARENCY TRACKING FORM

DATE: February 25, 2021

PACKET: 2015

DRUG: Trabectedin

USE: Malignant tumor of ovary; In combination with pegylated liposomal DOXOrubicin, following 1 or 2 previous platinum-based chemotherapy regimens

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 **advance** over current therapies
C	**Cancer** or cancer-related condition
E	Quantity and robustness of **evidence** for use support consideration
L	**Limited** alternative therapies exist for condition of interest
P	**Pediatric** condition
R	**Rare** disease
S	**Serious**, 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
Santaballa A, Barretina P, Casado A, García Y, González-Martín A, Guerra E, Laínez N, Martinez J, Redondo A, Romero I. SEOM Clinical Guideline in ovarian cancer (2016). Clin Transl Oncol. 2016 Dec;18(12):1206-1212.		S
Monk, BJ, Herzog, TJ, Kaye, SB, et al: Trabectedin plus pegylated liposomal Doxorubicin in recurrent ovarian cancer. J Clin Oncol Jul 01, 2010; Vol 28, Issue 19; pp. 3107-3114.	This was an international, open-label, randomized Phase 3 trial that assessed the addition of trabectedin to PLD as second-line therapy in women with recurrent ovarian cancer. The risk of potential bias associated with randomization, performance, detection, attrition, and reporting were deemed low. The risk of potential bias associated with allocation concealment was unclear due to the lack of information on these methods. An additional source of bias associated with trial funding was deemed low risk.	S
Monk, BJ, Herzog, TJ, Kaye, SB, et al: Trabectedin plus pegylated liposomal doxorubicin (PLD) versus PLD in recurrent ovarian cancer: overall survival analysis. Eur J Cancer Oct 2012; Vol 48, Issue 15; pp. 2361-2368.	This article contains final results from Monk et al 2010.	S
Monk, BJ, Herzog, TJ, Wang, G, et al: A phase 3 randomized, open-label, multicenter trial for safety and efficacy of combined trabectedin and pegylated liposomal doxorubicin therapy for recurrent ovarian cancer. Gynecol Oncol Mar 2020; Vol 156, Issue 3; pp. 535-544.	This was an international, open-label, randomized Phase 3 trial that assessed the addition of trabectedin to PLD for third-line therapy in women with recurrent ovarian cancer. The risk of potential bias associated with randomization, performance, detection, attrition, and reporting were deemed low. The risk of potential bias associated with allocation concealment was unclear due to the lack of information on these methods. An additional source of bias associated with trial funding was deemed low risk.	S

Colombo, N, Zaccarelli, E, Baldoni, A, et al: Multicenter, randomised, open-label, non-comparative phase 2 trial on the efficacy and safety of the combination of bevacizumab and trabectedin with or without carboplatin in women with partially platinum-sensitive recurrent ovarian cancer. Br J Cancer Oct 2019; Vol 121, Issue 9; pp. 744-750.		3
Krasner, CN, Poveda, A, Herzog, TJ, et al: Patient-reported outcomes in relapsed ovarian cancer: results from a randomized Phase III study of trabectedin with pegylated liposomal doxorubicin (PLD) versus PLD alone. Gynecol Oncol Oct 2012; Vol 127, Issue 1; pp. 161-167.		2
Lorusso, D, Gonzalez-Martin, A, and Ray-Coquard, I: Managing recurrent ovarian cancer in daily clinical practice: case studies and evidence review with a focus on use of trabectedin. Future Oncol Dec 23, 2020; Vol Epub, p. Epub.		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		
		Howard Goodman	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
IBM MICROMEDEX	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases		B
Richard LoCicero	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases	Three phase III trials have evaluated the use of pegylated liposomal doxorubicin in combination with trabectedin in ovarian cancer. Clinical benefit was observed in some populations (BRCA1/2 mutations and/or platinum free interval of 6-12 months). Response rates and progression free survival was observed in one trial, but not overall survival. Consensus guidelines support the use of the combination of trabectedin and pegylated liposomal doxorubicin in patients with a platinum free interval of 6 to 12 months, if a platinum-based regimen is not an option.	

Howard Goodman	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases	In the earliest paper cited, Monk et al 2010, the experimental arm suggested statistically significant benefit with respect to progression free interval and overall response rate accruing only in the patients felt to be platinum sensitive. Arguably the benefit in absolute terms was limited (7.3. vs. 5.8 months in PFS). In the recent review by Monk et al 2020, for third line therapy there was no evidence of benefit with regards to OS or PFS for the experimental arm in the entire cohort, at the price of significantly increased toxicity. However subgroup analysis demonstrated benefit in BRCA pos patients and specifically in BRCA pos patients who fell into the difficult 6-12 month platinum free interval. In the third paper cited, Monk et al 2012, again when the entire cohort was analyzed, there appeared to be no benefit, but again subgroup analysis demonstrated benefit in overall survival in those patients falling into the 6-12 month platinum free interval (22.4. vs 16.4 m). These analyses would suggest that there may be a limited role for this combination in patients with recurrent disease falling into the 6-12 month platinum free interval, who are not candidates for platinum therapy, and in patients with BRCA abnormalities, especially those who also fall into the 6-12 month platinum free interval.	
Jeffrey Klein	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases	The addition of Trabectedin to a pegylated liposomal doxorubicin regimen in advanced ovarian cancer patients demonstrated a good degree of PFS and ORR. The benefits of this combination were specific to patients who exhibit a specific cell mutation. The degree of neytropenia needs to be considered as well.	