IBM Watson Health

COMPENDIA TRANSPARENCY TRACKING FORM

DATE: 1/29/2020

PACKET: 1969

DRUG: Gemcitabine Hydrochloride

USE: Malignant tumor of nasopharynx; Locoregionally advanced disease, as induction therapy before chemoradiation

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)]

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EVIDENCE CONSIDERED:

*to meet requirements 2 and 4

CITATION	STUDY-SPECIFIC COMMENTS	LITERATURE CODE
Yuan, C, Xu, XH, Luo, SW, et al: Which neoadjuvant chemotherapy regimen should be recommended for patients with advanced nasopharyngeal carcinoma?: A network meta-analysis. Medicine (Baltimore) Aug 2018; Vol 97, Issue 34; p. e11978.		2
Zhang, Y, Chen, L, Hu, GQ, et al: Gemcitabine and cisplatin induction chemotherapy in nasopharyngeal carcinoma. N Engl J Med Sep 19, 2019; Vol 381, Issue 12; pp. 1124-1135.	This was an open-label, randomized Phase 3 clinical trial that assessed the addition of gemcitabine and cisplatin to standard chemoradiotherapy in patients with locoregionally advanced nasopharyngeal carcinoma. The risk of potential bias associated with randomization, attrition, and reporting were deemed low. The risk of bias associated with allocation concealment, performance, and detection were deemed high due to the open-label nature of the study. No other sources of bias were found.	S
Tan, T, Lim, WT, Fong, KW, et al: Concurrent chemo-radiation with or without induction gemcitabine, Carboplatin, and Paclitaxel: a randomized, phase 2/3 trial in locally advanced nasopharyngeal carcinoma. Int J Radiat Oncol Biol Phys Apr 01, 2015; Vol 91, Issue 5; pp. 952-960.	This was an open-label, randomized Phase 2/3 clinical trial that assessed the addition of induction gemcitabine, paclitaxel, and carboplatin to standard chemoradiotherapy in patients with locally advanced nasopharyngeal carcinoma. The risk of potential bias associated with randomization, attrition, and reporting were deemed low. The risk of bias associated with allocation concealment, performance, and detection were deemed high due to the open-label nature of the study. No other sources of bias were found.	S
Zhu, J, Duan, B, Shi, H, et al: Comparison of GP and TPF induction chemotherapy for locally advanced nasopharyngeal carcinoma. Oral Oncol Oct 2019; Vol 97, pp. 37-43.		1

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Liu, T, Sun, Q, Chen, J, et al: A comparison of neoadjuvant chemotherapy with gemcitabine versus docetaxel plus cisplatin in locoregionally advanced nasopharyngeal carcinoma: a propensity score matching analysis. Cancer Manag Res Nov 23, 2018; Vol 10, pp. 6237-6245.		1
Ma, J, Zhang, Y, Sun, Y, et al: Gemcitabine and cisplatin (GP) induction chemotherapy (IC) plus concurrent chemoradiotherapy (CCRT) versus CCRT alone in locoregionally advanced nasopharyngeal carcinoma (NPC): A phase 3, multicenter, randomized controlled trial. J Clin Oncol 2019; Vol 37, Issue Supp 15; p. 6003.		2

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		
Margi Schiefelbein, PA	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.

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ASSIGNMENT OF RATINGS:
*to meet requirement 4

	EFFICACY	STRENGTH OF RECOMMENDATION	COMMENTS	STRENGTH OF EVIDENCE
IBM MICROMEDEX	Evidence is Inconclusive	Class IIb: Recommended, in Some Cases		B
Richard LoCicero	Evidence is Inconclusive	Class IIb: Recommended, in Some Cases	Two randomized trials evaluated the use of gemcitabine in an induction regimen prior to definitive chemoradiation for the treatment of nasopharyngeal cancer. One trial demonstrated significantly improved 3-year recurrence-free survival, overall survival, and distant recurrence-free survival. However, one trial was not associated with improved 3-year overall survival, disease-free survival or distant metastases-free survival. Toxicity was increased with induction therapy. Therefore, there is evidence both supporting the use of induction therapy with gemcitabine and evidence demonstrating no clinical benefit.	
Jeffrey Klein	Evidence Favors Efficacy	Class IIa: Recommended, in Most Cases	The use of Gemcitabine (in a regimen for induction) before chemoradiation appears to offer a higher level of overall survival in one study. The incidence of serious adverse effects needs to be taken into consideration however.	
John Roberts	Evidence is Inconclusive	Class IIb: Recommended, in Some Cases	In a single trial gemcitabine + cisplatin induction chemotherapy followed by standard chemoradiotherapy improved overall survival as compared with standard chemoradiotherapy alone in locoregionally advanced nasopharyngeal carcinoma. A non-gemicitabine containing regimen has shown similar results. Of note, a trial of gemcitabine in combination with carboplatin and paclitaxel did not show a similar benefit. Nevertheless, evidence to date is less than conclusive. (1) The drop out rate in the single trial was quite asymmetric, and this asymmetry may have biased the results. (2) The epidemiology of nasopharyngeal carcinoma in China is quite different from the United States, suggesting that these may be different diseases, and, thus, raising concerns about the relevance of the single clinical trial. (3) In other head and neck cancers in the United States, multiple attempts to establish a role for induction chemotherapy have been unsuccessful.	

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