IBM Watson Health

COMPENDIA TRANSPARENCY TRACKING FORM

DATE: 6/18/2019

PACKET: 1901

DRUG: Nivolumab

USE: Malignant mesothelioma of pleura; Progressive or recurrent disease following platinum-based 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 **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
Scherpereel,A., Mazieres,J., Greillier,L., et al: Nivolumab or nivolumab plus ipilimumab in patients with relapsed malignant pleural mesothelioma (IFCT-1501 MAPS2): a multicentre, open-label, randomised, non-comparative, phase 2 trial. Lancet Oncol Feb 01, 2019; Vol 20, Issue 2; pp. 239-253.	This was an open-label, multi-center randomized, non-comparative trial that assessed second- and third-line nivolumab in patients with malignant pleural mesothelioma. Data were gathered prospectively for objective outcomes assessed by independent masked reviewers. The risk of potential bias associated with randomization, detection, attrition, and reporting were deemed low. The risk of potential biases associated with allocation concealment and performance were deemed high due to the open-label nature of the trial.	S
Disselhorst,M.J., Quispel-Janssen,J., Lalezari,F., et al: Ipilimumab and nivolumab in the treatment of recurrent malignant pleural mesothelioma (INITIATE): results of a prospective, single-arm, phase 2 trial. Lancet Respir Med 2019; Vol 7, Issue 3; pp. 260-270.	This was an open-label, single-center, single-arm phase II clinical trial that assessed Nivolumab plus ipilimumab in patients with malignant pleural mesothelioma. There was low risk of bias associated with selection of cohorts and assessment of outcomes. Data was gathered prospectively for objective outcomes, and assessed by an independent reviewer. All subjects with radiological assessment were included in the analyses. One caveat of the study is that it lacked a control group.	S
Quispel-Janssen,J., van der Noort,V, de Vries,J.F., et al: Programmed death 1 blockade with nivolumab in patients with recurrent malignant pleural mesothelioma. J Thorac Oncol Oct 2018; Vol 13, Issue 10; pp. 1569-1576.	This was an open-label, single-center, single-arm phase II clinical trial that assessed Nivolumab in patients with malignant pleural mesothelioma. There was low risk of bias associated with selection of cohorts and assessment of outcomes. Data was gathered prospectively for objective outcomes. All subjects with radiological assessment were included in the analyses. One caveat of the study is that it lacked a control group.	S
Woolhouse,I. and Maskell,N.A.: Introducing the new BTS guideline: the investigation and management of pleural malignant mesothelioma. Thorax Mar 01, 2018; Vol 73, Issue 3; pp. 210-212.		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
IBM MICROMEDEX	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases		B
John Roberts	Evidence is Inconclusive	Class III: Not Recommended	In two prospective trials in pleural mesothelioma, single agent nivolumab showed promising response rates of ~ 20%. Two factors render a recommendation to use premature. First, although in both trials nivolumab met the prospectively declared primary endpoint of landmark disease control rate, this endpoint is subject to significant patient selection bias; that is, failure to progress within a designated time frame may represent the natural history of the tumor unaffected by the drug, and the process of clinical trial enrollment tends to select for patients with more slowly growing tumors. In the absence of a randomized control, this sort of endpoint is not a reliable indicator of efficacy. Second, although in most contexts the primary benefit of immune checkpoint inhibitor therapy is durable response in a minority of patients, the survival curves from these trials do not suggest a significant fraction of durable responses. In general, toxicity was moderate.	

Jeffrey Klein	Evidence Favors Efficacy	Class IIa: Recommended, in Most Cases	The use of Nivolumab in 2nd line or greater patients to treat malignant mesolthelioma of pleura showed a good degree of efficacy. It appears that the use of nivolumab as monotherapy has similar efficacy to combination therapy. Though the safety profile of nivolumab seems to be tolerable, one study documented a 25% rate of higher grade adverse effects. The use of nivolumab as combination, or the more favorable monotherapy had a good overall response. The studies were small and the degree of higher grade adverse effects needs to be considered as not all patients are good candidates for nivolumab.	
Richard LoCicero	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases	Three phase II trials have demonstrated activity of nivolumab in the treatment of mesothelioma after prior therapy. Disease control rates ranged from 44% to 68%. No unexpected toxicities were observed. Clinical trial data has demonstrated clinical benefit. The noncomparative nature of these studies limit further conclusions, there for the class IIb recommendation.	