IBM Watson Health

COMPENDIA TRANSPARENCY TRACKING FORM

DATE: 7/16/2019

PACKET: 1906

DRUG: Dasatinib

USE: Philadelphia chromosome-positive acute lymphoblastic leukemia; Newly diagnosed, in combination with 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, E, 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
Ravandi F, Othus M, O'Brien SM, et al. US Intergroup Study of Chemotherapy Plus Dasatinib and Allogeneic Stem Cell Transplant in Philadelphia Chromosome Positive ALL. Blood Adv. 2016 Dec 27;1(3):250-259.	This was a multi-center, single-arm phase II clinical trial that assessed dasatinib in patients with newly diagnosed Philadelphia chromosome-positive ALL in the United States. There was low risk of bias associated with selection of cohorts and assessment of outcomes. Data was gathered prospectively for objective outcomes. All subjects were accounted for in the analyses. One caveat of the study is that it lacked a control or comparator group.	S
Ravandi,F., O'Brien,S.M., Corest,J.E., et al: Long-term follow-up of a phase 2 study of chemotherapy plus dasatinib for the initial treatment of patients with Philadelphia chromosome-positive acute lymphoblastic leukemia. Cancer Dec 01, 2015; Vol 121, Issue 23; pp. 4158-4164.		2
Rousselot,P., Coude,M.M., Gokbuget,N., et al: Dasatinib and low-intensity chemotherapy in elderly patients with Philadelphia chromosome-positive ALL. Blood Aug 11, 2016; Vol 128, Issue 6; pp. 774-782.	This was an international multi-center, single-arm phase II clinical trial that assessed dasatinib in patients with newly diagnosed Philadelphia chromosome-positive ALL. There was low risk of bias associated with selection of cohorts and assessment of outcomes. Data was gathered prospectively for objective outcomes. All subjects were accounted for in the analyses. One caveat of the study is that it lacked a control or comparator group.	S
Foa,R., Vitale,A., Vignetti,M., et al: Dasatinib as first-line treatment for adult patients with Philadelphia chromosome-positive acute lymphoblastic leukemia. Blood Dec 15, 2011; Vol 118, Issue 25; pp. 6521-6528.	This was a multi-center, single-arm phase II clinical trial that assessed dasatinib in patients with newly diagnosed Philadelphia chromosome-positive ALL in Italy. There was low risk of bias associated with selection of cohorts and assessment of outcomes. Data was gathered prospectively for objective outcomes. All subjects were accounted for in the analyses. One caveat of the study is that it lacked a control or comparator group.	S

Yoon,J.-H., Yhim,H.Y., Kwak,J.Y., et al: Minimal residual disease-based effect and long-term outcome of first-line dasatinib combined with chemotherapy for adult Philadelphia chromosomepositive acute lymphoblastic leukemia. Ann Oncol 2016; Vol 27, Issue 6; pp. 1081-1088.	This was a multi-center, single-arm phase II clinical trial that assessed dasatinib in patients with newly diagnosed Philadelphia chromosome-positive ALL in Korea. There was low risk of bias associated with selection of cohorts and assessment of outcomes. Data was gathered prospectively for objective outcomes. All subjects were accounted for in the analyses. One caveat of the study is that it lacked a control or comparator group.	S
Ravandi,F., O'Brien,S., Thomas,D., et al: First report of phase 2 study of dasatinib with hyper-CVAD for the frontline treatment of patients with Philadelphia chromosome-positive (Ph+) acute lymphoblastic leukemia. Blood Sep 23, 2010; Vol 116, Issue 12; pp. 2070-2077.		2
Sasaki,K., Jabbour,E.J., Ravandi,F., et al: Hyper-CVAD plus ponatinib versus hyper-CVAD plus dasatinib as frontline therapy for patients with Philadelphia chromosome-positive acute lymphoblastic leukemia: A propensity score analysis. Cancer Dec 01, 2016; Vol 122, Issue 23; pp. 3650-3656.		2
Hoelzer,D., Bassan,R., Dombret,H., et al: Acute lymphoblastic leukaemia in adult patients: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann.Oncol Sep 2016; Vol 27, Issue suppl 5; pp. v69-v82.	Guideline	S

Yilmaz,M., Kantarjian,H, Ravandi-Kashani,F., et al: Philadelphia chromosome-positive acute lymphoblastic leukemia in adults: current treatments and future perspectives. Clin Adv Hematol Oncol Mar 2018; Vol 16, Issue 3; pp. 216-223.		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 Favors Efficacy	Class IIb: Recommended, in Some Cases	The addition of bcr-abl targeted tyrosine kinase inhibitor therapy to standard chemotherapy in the treatment of newly diagnosed Philadelphia chromosome-positive acute lymphoblastic leukemia led to a consistent improvement in outcomes including remission rate and overall survival. All bcr-abl targeted tyrosine kinase inhibitors, including dasatinib, have shown similar improvements, but there are no comparative randomized trials. Toxicity profiles vary among the tyrosine kinase inhibitors. Almost all studies have involved cytotoxic chemotherapy, but one trial with reasonable results involved only dasatinib and prednisone. Optimal treatment probably varies according to patient fitness and co-morbidities, but there is little comparative data to guide clinical decision-making.	
Richard LoCicero	Effective	Class I: Recommended	Several trials have confirmed the efficacy of dasatinib (in combination with chemotherapy) in the treatment of Philadelphia chromosome-positive acute lymphoblastic leukemia.	
Jeffrey Klein	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases	The use of Dasatinib in newly diagnosed ALL patients that are Philadelphia chromosome positive shows a good degree of remission and complete remission data. Dasatinib is more effective in the younger patient subtype who undergo stem cell transplant. The advantage of dasatinib over other similar agents needs to be further evaluated.	