IBM Watson Health

COMPENDIA TRANSPARENCY TRACKING FORM

DATE: 5/7/2019

PACKET: 1864

DRUG: Rituximab

USE: Philadelphia chromosome-negative precursor B-cell acute lymphoblastic leukemia; CD20-positive, 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, 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
Maury,S., Chevret,S., Thomas,X., et al: Rituximab in B-Lineage adult acute lymphoblastic leukemia. N Engl J Med Sep 15, 2016; Vol 375, Issue 11; pp. 1044-1053.	This was an open-label, randomized safety and efficacy trial that included patients at 56 French and 9 Swiss clinical centers. Data were gathered prospectively for objective outcomes for the primary anallysis. The risks of potential bias associated with randomization, blinding of outcome assessment, attrition, and selective outcome reporting were all deemed low. The risks of potential bias associated with allocation concealment and blinding of participants and personnel were deemed high due to the open-label design of the trial. No additional biases were identified.	S
Thomas,D.A., O'Brien,S., Faderl,S., et al: Chemoimmunotherapy with a modified hyper-CVAD and rituximab regimen improves outcome in de novo Philadelphia chromosome-negative precursor B-lineage acute lymphoblastic leukemia. J Clin Oncol Aug 20, 2010; Vol 28, Issue 24; pp. 3880-3889.		3
Dinner,S. and Liedtke,M.: Antibody-based therapies in patients with acute lymphoblastic leukemia. Hematology Am Soc Hematol Educ Program Nov 30, 2018; Vol 2018, Issue 1; pp. 9-15.		4
Levato,L. and Molica,S.: Rituximab in the management of acute lymphoblastic leukemia. Expert Opin Biol Ther Feb 2018; Vol 18, Issue 2; pp. 221-226.		4

Hoelzer, D, Huettmann, A, Kaul, F, et al: Immunochemotherapy with rituximab improves molecular CR rate and outcome in CD20+ B-lineage standard and high risk patients; results of 263 CD20+ patients studied prospectively in GMALL Study 07/2003. Blood 2010; Vol 116, Issue 21; p. 170.		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 I: Recommended		B
Jeffrey Klein	Evidence Favors Efficacy	Class IIa: Recommended, in Most Cases	Adding Rituximab to a chemotherapy regimen to treat PH negative, CD20 positive ALL patients has a modest 2 year survival improvement then if not added. Rituximab appears to benefit “younger” patients who have low ECOG status. There is an increased rate of infection and infusion related effects with the Rituximab group.	
John Roberts	Evidence Favors Efficacy	Class I: Recommended	Rituximab added to combination chemotherapy and continued as maintenance in the treatment of adults with Philadelphia chromosome negative, CD20+ (20% of cells or greater) precursor B-cell acute lymphoblastic leukemia improved outcomes with a 12% decrease in relapse and a statistically significant 13% increase in event free survival, events being defined as remission induction failure, relapse, or death. A similar increase in survival was apparent but not statistically significant, although inspection of the survival curves suggests that this difference will persist and become statistically significant with the further passage of time. The survival curves also suggest that this difference represents an increment in cure rate. Additional toxicity was not discernible in the context of chemotherapy. It should be noted that ~ 1/3 of rituximab patients underwent allogeniec bone marrow transplantation in first remission. The relative roles of rituximab induction and maintenance are unknown.	
Richard LoCicero	Effective	Class I: Recommended	Rituximab has been shown to be effective in the treatment of CD20+ B-ALL by a phase III randomized trial in adults 18-59 years of age. No unexpected toxicity was observed.	