

COMPENDIA TRANSPARENCY TRACKING FORM

DATE: 6/13/2018

PACKET: 1695

DRUG: Asparaginase Escherichia Coli

USE: Extranodal NK/T-cell lymphoma, nasal type

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, 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
<p>Zhang,L., Jiang,M., Xie,L., et al: Five-year analysis from phase 2 trial of "sandwich" chemoradiotherapy in newly diagnosed, stage IE to IIE, nasal type, extranodal natural killer/T-cell lymphoma. Cancer Med Jan 01, 2016; Vol 5, Issue 1; pp. 33-40.</p>		S
<p>Wang,L., et al: Combination of gemcitabine, L-asparaginase, and oxaliplatin (GELOX) is superior to EPOCH or CHOP in the treatment of patients with stage IE/IIE extranodal natural killer/T cell lymphoma: a retrospective study in a cohort of 227 patients with long-term follow-up. Med Oncol Mar 2014; Vol 31, Issue 3; p. 860.</p>	<p>Comments: This was a retrospective study that compared three regimens in 227 patients who were newly diagnosed with stage I/II ENKTL. The median follow-up time for GELOX, EPOCH, and CHOP groups was 25.2 (range 9.9–59.8) months, 20.7 (range 4.4–102.6) months, and 25.7 (range 0.5–156.6) months, respectively. There was low risk of bias associated with selection of cohorts, comparability of cohorts, and assessment of outcome. The treatment response was assessed after every 2 cycles of chemotherapy or before and after radiotherapy in accordance with standard response criteria for non-Hodgkin lymphoma. After completion of treatment, patients were followed up by their oncologist in the outpatient department. Data was gathered from medical records. Statistical analyses were performed to control for the effect of potential confounding factors on outcomes. Twenty-one patients were lost to follow up, and complete survival data were available for the other 206 patients.</p>	S
<p>Jiang,M., et al: Phase 2 trial of "sandwich" L -asparaginase, vincristine, and prednisone chemotherapy with radiotherapy in newly diagnosed, stage IE to IIE, nasal type, extranodal natural killer/T-cell lymphoma. Cancer Jul 01, 2012; Vol 118, Issue 13; pp. 3294-3301.</p>	<p>Comments: This was a phase 2 study in patients who had previously untreated ENKTL. The median follow-up time for the 26 patients was 27 months (range, 4-35 months). All patients completed treatment according to the schedule. There was low risk of bias associated with selection of cohorts and assessment of outcome. Data was gathered prospectively. Statistical analyses were performed to control for the effect of potential confounding factors on outcomes. A major caveat of the study was that it included historical controls but did not provide any information or data from this group.</p>	S

<p>Kwong, Y.L., et al: SMILE for natural killer/T-cell lymphoma: analysis of safety and efficacy from the Asia Lymphoma Study Group. Blood Oct 11, 2012; Vol 120, Issue 15; pp. 2973-2980.</p>	<p>Comments: This was a phase 2 study in 43 newly diagnosed and 44 relapsed/refractory patients with natural killer/T-cell lymphoma. The study period was from March 2005 to February 2012. Median follow up was 31 months (1-84 months). All cases were analyzed on an intention-to-treat basis. Eighty-one patients (93%) received two courses of SMILE. There was low risk of bias associated with selection of cohorts and assessment of outcome. Data was gathered prospectively. Statistical analyses were performed to control for the effect of potential confounding factors on outcomes. A major caveat was the absence of a control group.</p>	<p>S</p>
<p>Jaccard, A., et al: Efficacy of L-asparaginase with mSethotrexate and dexamethasone (AspaMetDex regimen) in patients with refractory or relapsing extranodal NK/T-cell lymphoma, a phase 2 study. Blood Feb 10, 2011; Vol 117, Issue 6; pp. 1834-1839.</p>	<p>Comments: This was a phase 2 study in patients with relapsed or refractory extranodal NK/T-cell lymphoma. All the cases were centrally reviewed by 3 expert hematopathologists. Median follow-up among surviving patients was 26.2 months interquartile range (16.9-48.6 months). There was low risk of bias associated with selection of cohorts and assessment of outcome. Data was gathered prospectively. A major caveat was the absence of a control group.</p>	<p>S</p>
<p>d'Amore, F., et al: Peripheral T-cell lymphomas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol Sep 2015; Vol 26 Suppl 5, pp. v108-v115.</p>		<p>S</p>
<p>Jiang, M., et al: A phase II prospective study of the "Sandwich" protocol, L-asparaginase, cisplatin, dexamethasone and etoposide chemotherapy combined with concurrent radiation and cisplatin, in newly diagnosed, I/II stage, nasal type, extranodal natural killer/T-cell lymphoma. Oncotarget Jul 2017; Vol 8, Issue 30; pp. 50155-50163.</p>		<p>3</p>

<p>Wang,L., Q., et al: First-line combination of gemcitabine, oxaliplatin, and L-asparaginase (GELOX) followed by involved-field radiation therapy for patients with stage IE/IIe extranodal natural killer/T-cell lymphoma. Cancer Jan 15, 2013; Vol 119, Issue 2; pp. 348-355.</p>		<p>2</p>
<p>Li,J.-W., et al: Efficacy and tolerance of GELOXD/P-GEMOXD in newly diagnosed nasal-type extranodal NK/T-cell lymphoma: a multicenter retrospective study. Eur J Haematol Mar 01, 2018; Vol 100, Issue 3; pp. 247-256.</p>		<p>3</p>
<p>Dong,L.-H., et al: Sequential DICE combined with l-asparaginase chemotherapy followed by involved field radiation in newly diagnosed, stage IE to IIe, nasal and extranodal NK/T-cell lymphoma. Leuk Lymphoma Jul 2016; Vol 57, Issue 7; pp. 1600-1606.</p>		<p>3</p>
<p>Kim,M., et al: Ifosfamide, methotrexate, etoposide, and prednisolone (IMEP) plus l-asparaginase as a first-line therapy improves outcomes in stage III/IV NK/T cell-lymphoma, nasal type (NTCL). Ann Hematol Mar 01, 2015; Vol 94, Issue 3; pp. 437-444.</p>		<p>3</p>

<p>Pokrovsky, V.S. and Vinnikov, D.: L-Asparaginase for newly diagnosed extra-nodal NK/T-cell lymphoma: systematic review and meta-analysis. Expert Rev Anticancer Ther Aug 2017; Vol 17, Issue 8; pp. 759-768.</p>	<p>Comments: This was a systematic review that included 38 studies in which 11 were controlled trials and included in a meta-analysis. A major caveat of the study is that the authors did not present the characteristics of the included studies and they noted, "The main limitation of this meta-analysis, compromising free interpretation of our results, is the clinical heterogeneity across the studies, including different tumor stages, the standards of response rate assessment, the timelines for response evaluation, the doses of ASP and other agents, and the CT regimens." This systematic review conducted a comprehensive literature search and provided information on eligibility criteria, study characteristics, and heterogeneity. The appropriate statistical tests were used. The quality of the studies was assessed and varied greatly.</p>	<p>3</p>
<p>Wang, Y.Q., et al: Trial of LVDP regimen (L-asparaginase, etoposide, dexamethasone, and cisplatin, followed by radiotherapy) as first-line treatment for newly diagnosed, stage III/IV extranodal natural killer/T cell lymphoma. Med Oncol Feb 2015; Vol 32, Issue 2; p. 435.</p>		<p>3</p>
<p>Yamaguchi, M., et al: Phase II study of SMILE chemotherapy for newly diagnosed stage IV, relapsed, or refractory extranodal Natural Killer (NK)/T-cell lymphoma, nasal type: The NK-cell tumor study group study. J Clin Oncol Nov 20, 2011; Vol 29, Issue 33; pp. 4410-4416.</p>		<p>3</p>
<p>Bi, X.-W., et al: Consolidative treatment after salvage chemotherapy improved prognosis in patients with relapsed extranodal natural killer/T-cell lymphoma. Blood Dec 03, 2015; Vol 126, Issue 23; p. 5086.</p>	<p>Abstract</p>	<p>4</p>

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
Felicia Gelsey, MS	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
MICROMEDEX	Effective	Class I: Recommended		B
John D Roberts	Effective	Class I: Recommended	A variety of combination chemotherapy regimens incorporating Asparaginas Escherichia Coli have shown promising activity, including durable complete responses, in newly diagnosed, relapsed, and refractory Extranodal NK/T-cell lymphoma, nasal type. In patients with localized disease, a combination chemotherapy and radiation therapy approach has usually been used.	N/A

Jeffrey Klein	Evidence Favors Efficacy	Class IIa: Recommended, In Most Cases	The use of Asparaginase with various other agents, and in different chemotherapy regimens seems to be quite effective in treating T-cell lymphoma. All of the studies were small but all demonstrated a good degree of survival benefit. Somewhat concerning was the moderate degree of hematological toxicities reported that have the potential to delay or limit therapy. One study indicated that there was no control group which invalidates the trial it seems.	N/A
Richard LoCicero	Effective	Class I: Recommended	Several phase II and retrospective studies have established the efficacy of Asparaginase Escherichia Coli in combination regimens for the treatment of Extranodal NK/T-cell lymphoma, nasal type, with acceptable toxicity.	N/A