CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 22-249

STATISTICAL REVIEW(S)

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Translational Sciences
Office of Biostatistics

STATISTICAL REVIEW AND EVALUATION

CLINICAL STUDIES – TEAM LEADER'S MEMO

NDA/Serial Number:	22-249
Drug Name:	Bendamustine (Treanda)
Indication(s):	patients with (Binet Stage B/C) B-CLL requiring therapy
Applicant:	Cephalon
Date(s):	Submission date: September 20, 2007 PDUFA due date: March 20, 2008
Review Priority:	Priority (pilot for GRMP)
Biometrics Division:	Division of Biometrics 5 (HFD-711)
Primary Statistical Reviewer:	Shenghui Tang, Ph.D.
Secondary Reviewer:	Rajeshwari Sridhara, Ph.D., Team Leader/Deputy Division Director
Concurring Reviewer:	Aloka Chakravarty, Ph.D., Division Director
Medical Division:	Oncology Drug Products (HFD-150)
Clinical Team:	Qin Ryan, M.D., Ph.D., Virginia Kwitkowski,, M.S., RN., CRNP Amna Ibrahim, M.D. (CDTL)
Project Manager:	Ms. Dorothy Pease

Keywords: Co-primary endpoints, objective response rate, progression-free survival

Conclusion and Recommendation

This is Team Leader's memo of the New Drug Application (NDA) submission seeking approval for bendamustine (Treanda) as the first line treatment of chronic lymphocytic leukemia (CLL) based on one randomized study comparing to chlorambucil in previously untreated adults with symptomatic Binet stage B or stage C CLL requiring treatment. I concur with the primary reviewer, Dr. Tang's conclusion that the data submitted supports the claim that bendamustine has demonstrated superior overall response rate (ORR) and progression-free survival (PFS) compared to chlorambucil (ORR of 59% vs. 26% and PFS HR = 0.52, p-value < 0.0001). Please refer to the primary review by Dr. Tang for the details of the study and the results.

Progression-free survival was assessed by a panel of three independent expert hematologic oncologists and also objectively calculated using an algorithm based on NCI working group criteria. According to the sponsor, in performing the review the members of the independent panel were allowed to exercise clinical judgment in determining response and did not include bone marrow evaluations as required by the NCI working group criteria. The FDA reviewers were able to verify the calculated response rates and PFS, but could not verify the same as determined by the independent panel due the subjective nature of the independent evaluation. Therefore, it is recommended that the calculated response rates and PFS estimates be included in the product label.

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/s/

Rajeshwari Sridhara
2/25/2008 10:20:09 AM
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Aloka Chakravarty
2/25/2008 12:04:52 PM
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STATISTICAL REVIEW AND EVALUATION

CLINICAL STUDIES

NDA /Serial Number:	22-249
Drug Name:	Treanda
Applicant:	Cephalon
Indication(s):	Patients with (Binet Stage B/C) B-CLL Requiring Therapy
Date(s):	Submission Date: September 20, 2007 PDUFA Date: March 20, 2008 Review Completion Date: February 19, 2008
Review Priority:	Priority
Biometrics Division:	Division of Biometrics V (HFD-711)
Statistical Reviewer:	Shenghui Tang, Ph.D.
Concurring Reviewer:	Rajeshwari Sridhara, Ph.D., Team Leader Aloka Chakravarty, Ph.D., Director
Medical Division:	Oncology Drug Products (HFD-150)
Clinical Team:	Qin Ryan, M.D., Virginia Kwitkowski, M.D. Amna Ibrahim, M.D.
Project Manager:	Ms. Dorothy Pease
Keywords:	Objective response rate, Duration of response, PFS

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