

Food and Drug Administration
Center for Drug Evaluation and Research
Oncologic Drugs Advisory Committee (ODAC) Meeting
FDA White Oak Campus, Building 31, the Great Room, White Oak Conference Center
(Rm. 1503), Silver Spring, MD

July 14, 2011

DRAFT QUESTIONS

BLA 125399
Adcetris (brentuximab vedotin) for injection

APPLICANT: Seattle Genetics, Inc.

PROPOSED INDICATION: for the treatment of relapsed or refractory systemic anaplastic large cell lymphoma (ALCL).

Seattle Genetics, Inc. submitted a biologics licensing application, BLA 125399, for the treatment of patients with relapsed or refractory systemic anaplastic large cell lymphoma (ALCL). The primary basis for this application is clinical trial SG035-0004, a single-arm Phase 2 clinical trial. The study population consisted of patients with Anaplastic Large cell Lymphoma who relapse. Brentuximab vedotin was given intravenously at a dose of 1.8 mg/kg every 21 days for up to 16 cycles.

The primary endpoint was Objective Response Rate (ORR), and the key secondary endpoints were Duration of Response and Complete Remission (CR) Rate. Responses were determined by an Independent Review Facility (IRF) using Sponsor-modified 2007 Revised Response Criteria for Malignant Lymphoma.

SG035-0004 enrolled a total of 58 patients. Seventy-eight percent of the patients were between the ages of 18 to 64. Patients had either relapsed or recurrent disease and the median number of prior systemic therapies was two. Overall response rate was 86% with a median duration of 12.6 months. CR rate was 57% with a median duration of 13.2 months. Partial remission rate was 29% with a median duration of 2.1 months. Peripheral neuropathy and myelosuppression were the most common adverse events identified by the Sponsor.

The single arm design and small size limits the benefit-risk analysis. Efficacy results are limited to response rates and duration of responses. Time-to-event endpoints such as progression-free survival or overall survival cannot be adequately interpreted in a single arm trial. In addition, a single arm trial does not permit attribution of the adverse events.

The Sponsor was advised by the FDA as early as 2008 that a response rate with prolonged duration and an acceptable risk-benefit may support an accelerated approval.

For this application, consideration for accelerated approval would be consistent with regulatory actions taken in the past decade for similar hematology applications based on single arm clinical trials.

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DRAFT QUESTIONS (continued)

1. **VOTE:** The FDA has identified limitations of trial SG035-0004. Should the FDA grant accelerated, regular or non-approval for brentuximab vedotin in the treatment of patients with relapsed systemic ALCL?
 - A. ACCELERATED APPROVAL
 - B. REGULAR APPROVAL
 - C. NO APPROVAL
 - D. ABSTAIN

2. **DISCUSS:** If the Agency were to grant accelerated approval for brentuximab vedotin, please discuss potential confirmatory studies. Please discuss endpoints and comparators.

DRAFT