S200 IMPROVED OVERALL SURVIVAL WITH FIRST-LINE BRENTUXIMAB VEDOTIN PLUS CHEMOTHERAPY IN PATIENTS WITH STAGE III/IV CLASSICAL HODGKIN LYMPHOMA: 6-YEAR ANALYSIS OF ECHELON-1

Topic: 17. Hodgkin lymphoma - Clinical

Martin Hutchings1, Stephen M. Ansell2, David J. Straus3, Joseph M. Connors4, Won Seog Kim5, Andrea Gallamini6, Radhakrishnan Ramchandren7, Jonathan W. Friedberg8, Ranjana Advani9, Andrew M. Evans10, Piotr Smolewski11, Kerry J. Savage4, Nancy L. Bartlett12, Hyeon-Seok Eom13, Jeremy S. Abramson14, Cassie Dong15, Frank Campana15, Keenan Fenton16, Markus Puhlmann16, John Radford17

1 Department of Haematology, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark; 2 Division of Hematology, Mayo Clinic, Rochester, MN, United States; 3 Department of Medicine, Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York, NY, United States; 4 BC Cancer Centre for Lymphoid Cancer and Department of Medical Oncology, Vancouver, Canada; 5 Division of Hematology-Oncology, Department of Internal Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, Republic Of; 6 Research and Innovation, Antoine-Lacassagne Cancer Centre, Nice, France; 7 The University of Tennessee Graduate School of Medicine, Knoxville, TN, United States; 8 James P. Wilmot Cancer Institute, University of Rochester Medical Center, Rochester, NY, United States; 9 Department of Medicine, Division of Oncology, Stanford University, Stanford, CA, United States; 10 Division of Blood Disorders, Rutgers Cancer Institute of New Jersey, New Brunswick, NJ, United States; 11 Department of Experimental Hematology, Medical University of Lodz, Lodz, Poland; 12 Washington University School of Medicine Siteman Cancer Center, St Louis, MO, United States; 13 Center for Hematologic Malignancy, National Cancer Center, Goyang, Korea, Republic Of; 14 Massachusetts General Hospital, Boston, MA, United States; 15 Takeda Development Center Americas, Inc. (TDCA), Lexington MA, United States; 16 Seagen Inc., Bothell, WA, United States; 17 The University of Manchester and the Christie NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, United Kingdom

Background: In classical Hodgkin lymphoma (cHL), improved overall survival (OS) with first-line treatment using new combinations has seldom been observed compared with existing approaches. Five-year data from the randomized phase 3 ECHELON-1 study (NCT01712490) supported long-term progression-free survival (PFS) with brentuximab vedotin, doxorubicin, vinblastine, and dacarbazine (A+AVD) versus doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD), in patients (pts) with previously untreated stage III/IV cHL, regardless of interim positron emission tomography (PET) status. The long-term safety profile of A+AVD was manageable, and numerically fewer secondary malignancies were reported versus ABVD, as well as a greater number of pregnancies (Straus et al, Lancet Haematol 2021).

Aims: To report the pre-specified OS analysis from ECHELON-1, as well as relevant long-term safety data, after approximately 6 years of follow-up (cut-off June 1, 2021).

Methods: Pts were randomized 1:1 to receive up to 6 cycles of A+AVD (n=664) or ABVD (n=670) on day 1 and 15, every 28 days. PFS per investigator was reported for long-term follow-up. The key secondary end point was OS, which was an event-driven, pre-specified, alpha-controlled analysis in the intention-to-treat population, with a prespecified interim analysis after 103 deaths. Analysis of OS in prespecified subgroups was exploratory and was not adjusted for multiplicity. Informed consent was obtained for all pts.

Results: In total, 39 OS events in the A+AVD arm and 64 in the ABVD arm had occurred at a median follow-up of 73 months, significantly favoring A+AVD (hazard ratio [HR] 0.590; 95% CI 0.396–0.879; p=0.009). There was a consistent OS benefit for A+AVD vs ABVD across prespecified subgroups, including: stage III (HR: 0.863; 95% CI 0.452–1.648) and stage IV disease (HR: 0.478; 95% CI 0.286–0.799) at diagnosis, pts who were PET-negative at interim positron emission tomography (PET2)-negative (HR: 0.583; 95% CI 0.338–0.856) and PET2-positive (HR: 0.163; 95% CI 0.037–0.717), pts aged <60 years (HR: 0.509; 95% CI 0.291–0.890), pts aged ≥60 years (HR: 0.829; 95% CI 0.469–1.466), and across all geographies, including Europe (HR: 0.783; 95% CI 0.467–1.315) and North America (HR: 0.327; 95% CI 0.153–
The 6-year PFS estimate was 82.3% (79.1–85.0) vs 74.5% (70.8–77.7) with A+AVD vs ABVD, respectively (HR: 0.678; 95% CI: 0.532–0.863). The long-term safety profile of A+AVD was comparable to that of ABVD. In both A+AVD and ABVD groups, treatment-emergent peripheral neuropathy continued to resolve or improve, with 86% (379/443) and 87% (249/286) of cases in the A+AVD and ABVD arms either completely resolving (72% vs 79%) or improving (14% vs 8%) by last follow-up. Overall, 23 secondary malignancies in the A+AVD arm and 32 in the ABVD arm were reported. Pregnancies and live births were reported by a greater number of female pts in the A+AVD group vs the ABVD group (49 vs 28 and 42 vs 19, respectively) and there were no stillbirths reported during the study. There were no new safety signals.

**Summary/Conclusion:** There was a statistically significant 41% reduction in the risk of death with A+AVD vs ABVD, with a consistent OS benefit across prespecified subgroups. The long-term safety profile was manageable, consistent with prior reports. These data support A+AVD as a preferred option for previously untreated stage III and IV cHL.

© American Society of Clinical Oncology, Inc. Reused with permission. This abstract was accepted and previously presented at the 2022 ASCO Annual Meeting. All rights reserved.