EHA2021 VIRTUAL

S189

UPDATED RESULTS FROM PHASE 3 ANDROMEDA STUDY OF PATIENTS WITH NEWLY DIAGNOSED LIGHT CHAIN AMYLOIDOSIS TREATED WITH BORTEZOMIB, CYCLOPHOSPHAMIDE, AND DEXAMETHASONE PLUS SUBCUTANEOUS DARATUMUMAB

Topic: 14. Myeloma and other monoclonal gammopathies - Clinical

Keywords: Amyloidosis

Efstathios Kastritis[1], Vaishali Sanchorawala[2], Giovanni Palladini[3], Monique Minnema[4], Ashutosh Wechalekar[5], Arnaud Jaccard[6], Angela Dispenzieri[7], Hans Lee[8], Divaya Bhutani[9], Simon Gibbs[10], Peter Mollee[11], Christopher Venner[12], Jin Lu[13], Stefan Schönland[14], Moshe Gatt[15], Kenshi Suzuki[16], Kihyun Kim[17], Teresa Cibeira[18], Meral Beksac[19], Edward Libby[20], Jason Valent[21], Vania Hungria[22], Sandy Wong[23], Michael Rosenzweig[24], Naresh Bumma[25], Dominique Chauveau[26], NamPhuong Tran[27], Xiang Qin[28], Sandra Vasey[28], Brenda Tromp[29], Brendan Weiss[28], Jessica Vermeulen[29], Raymond Comenzo[30], Giampaolo Merlini[3]

[1] National and Kapodistrian University of Athens, Athens, Greece
[2] Boston University School of Medicine and Boston Medical Center, Boston, United States
[3] Fondazione Istituto di Ricovero e Cura a Carattere Scientifico Policlinico San Matteo and University of Pavia, Pavia, Italy
[4] University Medical Center Utrecht, Utrecht, Netherlands
[5] University College London, London, United Kingdom
[6] Centre Hospitalier Universitaire and Reference Center for AL Amyloidosis, Limoges, France
[7] Mayo Clinic, Rochester, United States
[8] The University of Texas MD Anderson Cancer Center, Houston, United States
[9] Columbia University Medical Center, New York, United States
[10] Monash University Eastern Health Clinical School, Melbourne, Australia
[11] Princess Alexandra Hospital and University of Queensland Medical School, Brisbane, Australia
[12] Cross Cancer Institute, University of Alberta, Edmonton, Canada
[13] Peking University People's Hospital, Peking University Institute of Hematology, Beijing, China
[14] Amyloidosis Center, Heidelberg University Hospital, Heidelberg, Germany
[15] Hadassah Hebrew University Medical Center, Jerusalem, Israel
[16] Japanese Red Cross Medical Center, Tokyo, Japan
[17] Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, Democratic People's Republic Of
[18] Hospital Clinic of Barcelona, Barcelona, Spain
[19] Ankara University, Ankara, Turkey
[20] University of Washington, Seattle, United States
[21] Taussig Cancer Center, Cleveland Clinic, Cleveland, United States
[22] Clinica Sao Germano, Sao Paulo, Brazil
[23] University of California San Francisco, San Francisco, United States
[24] Judy and Bernard Briskin Center for Multiple Myeloma Research, Duarte, United States
[25] The Ohio State University Comprehensive Cancer Center, Columbus, United States
[26] CHU de Toulouse-Hôpital Rangueil, Toulouse, France
[27] Janssen Research & Development, LLC, Los Angeles, United States
[28] Janssen Research & Development, LLC, Spring House, United States
[29] Janssen Research & Development, LLC, Leiden, Netherlands
[30] John C. Davis Myeloma and Amyloid Program, Tufts Medical Center, Boston, United States

Background: Light chain amyloidosis (AL) is a systemic plasma cell disease where organ impairment and death

can occur due to insoluble amyloid fibrils deposition. Adding subcutaneous daratumumab to the standard of care (bortezomib, cyclophosphamide, and dexamethasone [VCd]) in ANDROMEDA (NCT03201965) led to superior outcomes versus VCd alone (primary results), including greater hematologic complete response (CR) rates and an acceptable safety profile. In January 2021, Daratumumab+VCd was approved for patients with newly diagnosed AL amyloidosis.

Aims: To report updated primary results with longer follow up from the ANDROMEDA study.

Methods: ANDROMEDA is an ongoing open-label, randomized, active-controlled, phase 3 trial. Adult patients with newly diagnosed AL amyloidosis were randomly assigned 1:1 to receive daratumumab+VCd or VCd for six 28-day cycles. Written informed consent was obtained from all patients. Bortezomib dosed at 1.3 mg/m^2, cyclophosphamide at 300 mg/m^2 (up to 500 mg weekly), and dexamethasone at 40 mg were administered every week. Subcutaneous daratumumab was administered once weekly in cycles 1 and 2 and every 2 weeks in cycles 3 to 6. Patients in the daratumumab+VCd arm received only subcutaneous daratumumab after cycle 6, every 4 weeks (up to a total of 24 cycles from first dose). Disease status was assessed every 4 weeks in cycles 1 to 6 and every 8 weeks thereafter. Overall hematologic CR rate (intent-to-treat population) was the primary endpoint. Time to hematologic response, major organ deterioration progression-free survival, survival, organ response rate, and safety were the secondary endpoints.

Results: Among 388 randomized patients, 195 received daratumumab+VCd and 193 received VCd alone. At the November 2020 cutoff, the median duration of treatment for daratumumab+VCd and VCd arms was 18.5 and 5.3 months, respectively, and 78 patients (40%) in the daratumumab+VCd arm were still receiving treatment. The overall hematologic CR rate in the daratumumab+VCd arm (59%) was significantly higher versus the VCd arm (19%; odds ratio [95% CI], 5.9 [3.7–9.4]; P<0.0001). More patients achieved a very good partial response or better (≥VGPR) with daratumumab+VCd (79%) compared with VCd alone (50%; odds ratio [95% CI], 3.7 [2.4–5.9]; P<0.0001). Among patients who responded, the median time from randomization to ≥VGPR was shorter in the daratumumab+VCd arm (0.56 months) versus the VCd arm (0.82 months). Greater cardiac response rates were achieved at 6 months with daratumumab+VCd (42%) versus VCd alone (22%) and at 12 months (57% versus 28%); similarly, renal response rates were greater with daratumumab+VCd (54%) versus VCd alone (27%) at 6 months and at 12 months (57% versus 27%). Overall, 71 patients died (daratumumab+VCd, 31; VCd, 40). Starting cycle 7, no grade 3/4 treatment-emergent adverse events occurred in ≥5% of patients in the daratumumab+VCd arm. After cycle 6, no systemic administration-related reactions were reported with in the daratumumab+VCd. Major organ deterioration progression-free survival is scheduled to be updated after approximately 200 events.

Summary/Conclusion: Updated results from the ANDROMEDA study further support that in patients with newly diagnosed AL amyloidosis, the daratumumab+VCd combination is clinically superior compared with VCd alone. Following its recent approval, the daratumumab+VCd combination represents a new standard of care for patients with AL amyloidosis.

Abstract Book Citations: Authors, Title, HemaSphere, 2021;5:(S2):pages. Abstract Book, DOI:
http://dx.doi.org/10.1097/HS9.0000000000000566