PET4 Response as an Independent Predictor of Outcomes in ECHELON-2 A+CHP vs CHOP in CD30+ PTCL: Intent to Treat Analysis

Swaminathan Iyer[1], Neha Mehta-Shah[2], Ranjana Advani[3], Nancy Bartlett[2], Jakob Christensen[4], Franck Morschhauser[5], Eva Domingo-Domenech[6], Giuseppe Rossi[7], Won Seog Kim[8], Onder Alpdogan[9], Cheolwon Suh[10], Tatyana Feldman[11], Herve Tilly[12], Alessandro Rambaldi[13], Pier Luigi Zinzani[14], David Belada[15], Jiri Mayer[16], Ilseung Choi[17], June Weon Cheong[18], Shweta Jain[19], Keenan Fenton[19], Michelle Fanale[19], Kerry Savage[20], Steve Horwitz[21]

[1]MD Anderson Cancer Center/University of Texas, Houston, TX, USA; [2]Washington University School of Medicine, St. Louis, MO, USA; [3]Stanford Cancer Center, Blood and Marrow Transplant Program, Stanford, CA, USA; [4]Odense University Hospital, Odense, Denmark; [5]CHRU de Lille, Lille cedex, Nord-Pas-de-Calais, France; [6]Institut Catala D'oncologia, L'Hospitalet de Llobregat, Barcelona, Spain; [7]Azienda Ospedaliera Spedali Civili di Brescia, Brescia, Italy; [8]Sungkyunkwan University School of Medicine, Samsung Medical Center, Seoul, Republic of Korea; [9]Thomas Jefferson University, Philadelphia, PA, USA; [10]Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; [11]Hackensack University Medical Center, Hackensack, NJ, USA; [12]Department of Hematology and INSERM Unité 1245, Centre Henri-Becquerel and University of Rouen, Rouen, France; [13]University of Milan and Azienda Socio Sanitaria Territoriale Papa Giovanni XXIII, Bergamo, Italy; [14]Institute of Hematology "Seràgnoli" University of Bologna, Bologna, Italy; [15]Charles University, Hospital and Faculty of Medicine, Hradec Králové, Czech Republic; [16]University Hospital Brno, Brno, Czech Republic; [17]National Hospital Organization Kyushu Cancer Center, Fukuoka, Japan; [18]Yonsei University College of Medicine, Seoul, Republic of Korea; [19]Seagen Inc., Bothell, WA, USA; [20]BC Cancer Centre for Lymphoid Cancer and The University of British Columbia, Vancouver, BC, Canada; [21]Memorial Sloan Kettering Cancer Center, New York, NY, USA

Objective

The objective of this exploratory analysis was to evaluate the role of interim 18F-FDG PET imaging in predicting EOT response, PFS, and OS in patients with CD30+ PTCL treated with A+CHP or CHOP in the ECHELON-2 trial.

Conclusions

- PET4neg as assessed by Deauville score was associated with improved PFS and OS in both the A+CHP and CHOP arms.
- Our findings support the use of PET4 response in PTCL as a predictor of outcomes in both the A+CHP- and CHOP-treated patients.
- These findings emphasize the potential of PET scans to enhance risk stratification, individualize therapy decisions, and improve patient outcomes in the management of patients with PTCLs.
- A limitation of the current analysis is that this exploratory subgroup analysis was post-hoc, which may introduce unknown bias.

Abbreviations

18F-FDG, fludeoxyglucose (18F); A+CHP, brentuximab vedotin plus cyclophosphamide, doxorubicin, and prednisone; AE, adverse event; AITL, angioimmunoblastic T-cell lymphoma; ALCL, anaplastic large-cell lymphoma; ALK, anaplastic lymphoma kinase; ATLL, adult T-cell leukemia/lymphoma; CD30+ PTCL, CD30-positive peripheral T-cell lymphomas; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; CI, confidence interval; CR, complete response; EATL, enteropathy-associated T-cell lymphoma; ECOG, Eastern Cooperative Oncology Group; EOT, end of treatment; HR, hazard ratio; HSTCL, hepatosplenic T-cell lymphoma; IPI, international prognostic index; IRF, independent review facility; OS, overall survival; PET, positron emission tomography; PET4, 18F-FDG PET scans at cycle 4; PD, progressive disease; PFS, progression-free survival; PR, partial response; PTCL, peripheral T-cell lymphomas; R, randomization; sALCL, systemic anaplastic large-cell lymphoma; SD, stable disease

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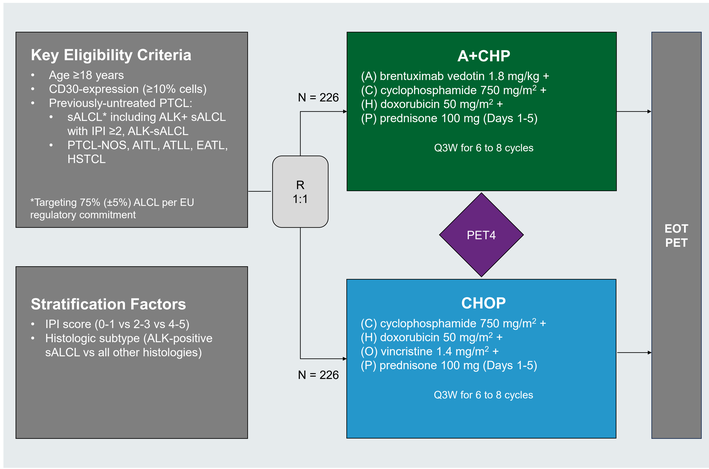
Background

- PTCLs are uncommon, heterogeneous, and often aggressive subtypes of lymphoma characterized by a high risk of progression, even after combination chemotherapy.[1,2]
- The phase 3, ECHELON-2 trial showed that A+CHP in patients with CD30+ PTCLs had significantly improved PFS (HR, 0.70 [95% CI, 0.53-0.91], P=0.0077) and OS (HR, 0.72 [95% CI, 0.53-0.99], P=0.0424) compared with CHOP.[3,4]
- In PTCL, PET is a valuable way to assess disease burden and stage at the time of diagnosis and evaluate treatment response.[5,6]
- Prior retrospective studies have shown that interim and EOT PET scans may predict outcomes[7,8]; however, there are no prospective studies confirming their predictive value.
- In the ECHELON-2 study, PET4 (18F-FDG PET scans at cycle 4) was assessed.

Methods

- ECHELON-2 (NCT01777152) was a double-blind, double-dummy, randomized, placebo-controlled, active comparator phase 3 study[3,4] (**Figure 1**).
- The ECHELON-2 trial included 18F-FDG PET scans at cycle 4 and assessment of treatment response, including long-term PFS per investigator and OS.
- PET4 assessment outcome was determined by Deauville score by IRF assessment using scans at the cycle 4 response assessment.
- Deauville scores of 1-3 are considered negative (PET4neg) and 4-5 positive (PET4pos).[9]
- EOT response was the best response after completion of study treatment and prior to long-term follow-up per the Revised Response Criteria for Malignant Lymphoma[10] by IRF assessment.
- Kaplan-Meier methods were used to estimate PFS and OS by PET4 status in the overall population and in the sALCL subgroup; P values are based on stratified log-rank tests. All analyses are exploratory, and P values are descriptive.
- Safety data for ECHELON-2 has been previously described.[3,4]

Figure 1. Study Design



Results

Baseline Characteristics

- A total of 452 patients were randomized to A+CHP (n = 226) or CHOP (n = 226); median follow up was 66.8 months (range 0-90).
- Baseline patient demographics and disease characteristics were balanced between treatment arms as previously described.[3]

Efficacy by PET4 Status in the Overall Population

- Of the 226 patients in each treatment arm, 32 patients in the A+CHP arm and 41 patients in the CHOP arm were not evaluable for PET4. This included patients who discontinued treatment early due to AE or PD.
- Of the PET4-evaluable patients in the overall population, 175/194 (90%) in the A+CHP arm and 147/185 (79%) in the CHOP arm were PET4neg.
- Among the PET4-evaluable patients in the A+CHP arm, the PET4neg subgroup had a higher CR rate (142/175 [81%]) than PET4pos (1/19; [5%]) at EOT (**Figure 2**).
- Among the PET4-evaluable patients in the CHOP arm, the PET4neg subgroup had a higher CR rate (115/147; [78%]) than PET4pos (4/38; [11%]) at EOT (**Figure 2**).
- PET4neg patients in both treatment arms had improved PFS (**Figure 3**) and OS (**Figure 4**) compared to those who were PET4pos.

Efficacy by PET4 Status in the sALCL Subgroup

- Among 316 patients with sALCL, 19 in the A+CHP arm and 32 in the CHOP arm were not evaluable for PET4.
- Of the PET4-evaluable patients in the sALCL subgroup, 128/143 (90%) in the A+CHP arm and 98/122 (80%) in the CHOP arm were PET4neg.
- PET4neg patients in both treatment arms had improved PFS (**Figure 5**) and OS (**Figure 6**) compared to those who were PET4pos.

Figure 2. Cycle 4 PET Status and EOT Response

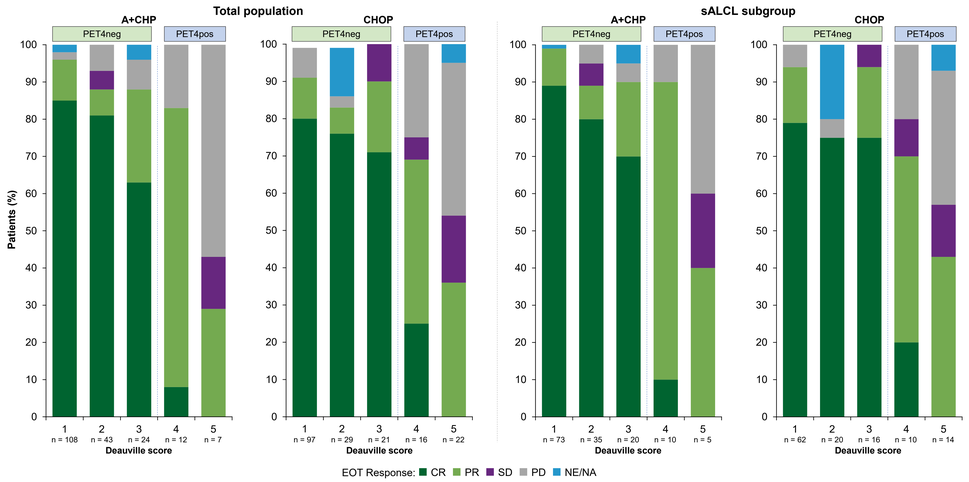


Figure 3. PFS by Cycle 4 PET Status in the A+CHP (A) and CHOP (B) arms

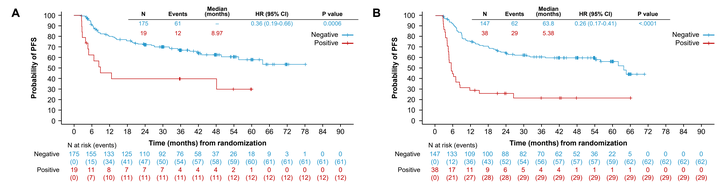


Figure 4. OS by Cycle 4 PET Status in the A+CHP (A) and CHOP (B) arms

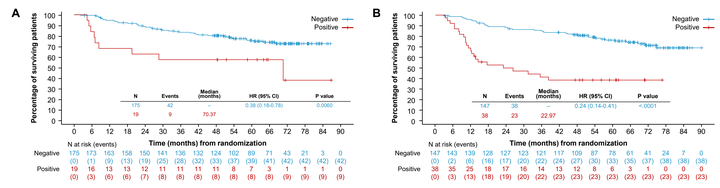


Figure 5. PFS by Cycle 4 PET Status in the A+CHP (A) and CHOP (B) arms (sALCL subgroup)

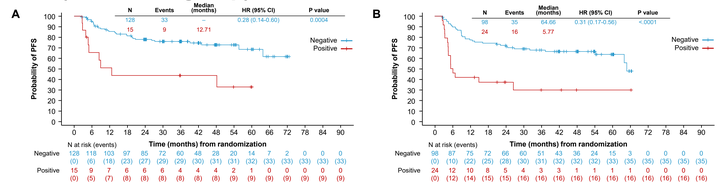


Figure 6. OS by Cycle 4 PET Status in the A+CHP (A) and CHOP (B) arms (sALCL subgroup)