FRONTLINE BRENTUXIMAB VEDOTIN AND CHP (A+CHP) IN SUBJECTS WITH PERIPHERAL T-CELL LYMPHOMA WITH LESS THAN 10% CD30 EXPRESSION

(TRIAL IN PROGRESS)
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Brentuximab Vedotin Description and MOA

- Brentuximab vedotin (BV, ADCETRIS®) is an antibody-drug conjugate composed of an anti-CD30 monoclonal antibody conjugated by a protease-cleavable linker to the microtubule-disrupting agent, monomethyl auristatin E (MMAE)
- Targeted delivery of MMAE to CD30-expressing cells is the primary mechanism of action of BV[1]
- Binding of MMAE to tubulin disrupts the microtubule network within the cell, subsequently inducing cell cycle arrest and apoptotic death of the cell
- Direct cytotoxicity associated with BV may be augmented by secondary effects, including the bystander effect[2] and several important immuno-oncology related effects, such as immunogenic cell death[3,4] and antibody-dependent cellular phagocytosis[5]

1) Sutherland MS et al. J Biol Chem. 2006;281(15):10540-7. 2) Li et al. Cancer Res. 2016;76(9):2710-9. 3) Gardai SJ et al. Haematologica. 2016;101(S5):53. 4) Muller P et al. Cancer Immunol Res. 2014;2(8):741-55. 5) Oflazoglu E et al. Blood. 2007;110(13):4370-2.

Background and Rationale

- ECHELON-2 phase 3 clinical trial:
  - BV, cyclophosphamide, doxorubicin, and prednisone (A+CHP) showed clinically meaningful and statistically significant efficacy in subjects with peripheral T-cell lymphoma (PTCL) across a range of CD30 expression levels, including the lowest eligible level of 10% by IHC when compared with subjects treated with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) alone. [6]
  - No significant increase in toxicity was observed.[6]
  - Trial led to FDA approval of A+CHP in subjects with previously untreated, CD30-expressing PTCL.

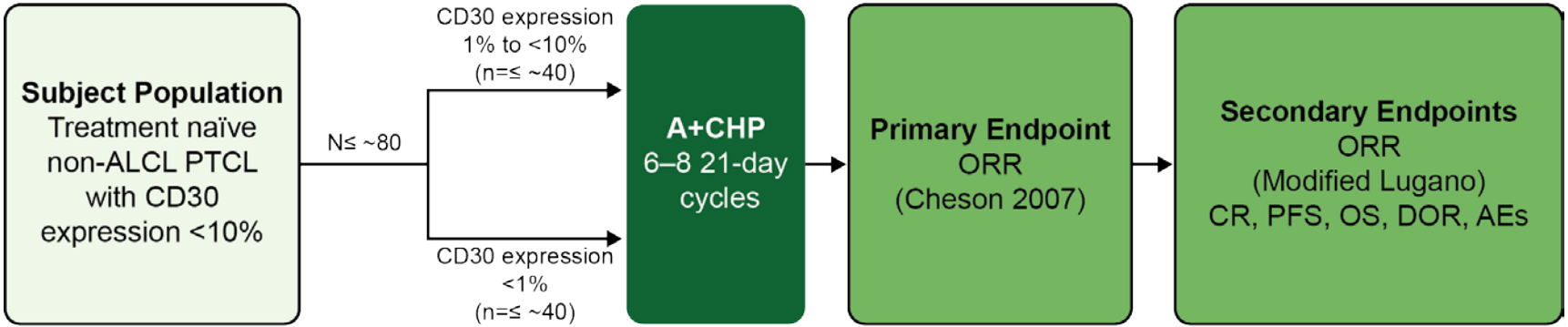
6) Horwitz S et al. Lancet. 2019;393(10168):229-40.

Background and Rationale

- Response data from other trials are available from 344 subjects
  - Subjects had CD30-expressing PTCL and other large-cell lymphomas (including angioimmunoblastic T-cell lymphoma and peripheral T-cell lymphoma-NOS) and had been treated in studies with BV as a single agent or in combination with chemotherapy, in both frontline and relapsed/refractory settings.[7]
  - 184 subjects had tumors with CD30 expression <10% by local assessment
    - Including 83/184 subjects with undetectable CD30 by immunohistochemistry (CD30=0).
  - Responses to BV observed at all levels of CD30 expression, including in tumors with undetectable CD30 levels.[6,7]

6) Horwitz S et al. Lancet. 2019;393(10168):229-40. 7) Advani RH et al. J Clin Oncol. 2019;37(Suppl 15):Abstract 7538.

Study Design



Assessments

- Efficacy assessments by blinded independent central review (BICR) using Revised Response Criteria for Malignant Lymphoma and modified Lugano criteria
- Safety assessments include surveillance and recording of AEs and concomitant medications, physical examination findings, and laboratory tests

Study Objectives

Primary Objectives	Primary Endpoints
• To evaluate the objective response rate (ORR) per BICR using Revised Response Criteria for Malignant Lymphoma criteria[8]	• ORR per BICR following the completion of study treatment using Revised Response Criteria for Malignant Lymphoma criteria[78]

Secondary Objectives	Secondary Endpoints
• To evaluate the complete response (CR) rate following completion of study treatment[8] • To evaluate the progression-free survival PFS[8] • To evaluate overall survival (OS) • To evaluate duration of response (DOR) [8] • To evaluate ORR per BICR, using modified Lugano criteria[9] • To evaluate the safety and tolerability	• CR rate per BICR[8] • PFS per BICR[8] • OS • DOR per BICR • ORR per BICR, using modified Lugano criteria[9] • Type, incidence, severity, seriousness, and relatedness of adverse events (AEs) • Laboratory abnormalities

8) Cheson BD et al. J Clin Oncol. 2007;25(5):579-86. 9) Cheson BD et al. J Clin Oncol. 2014;32(27):3059-68.

Eligibility

Key Inclusion Criteria

- Adults with newly diagnosed PTCL, excluding systemic anaplastic large cell lymphoma (sALCL), per the WHO 2016 classification
- CD30 expression <10% by local assessment
- PTCL histology
  - PTCL – not otherwise specified (PTCL-NOS)
  - Angioimmunoblastic T-cell lymphoma (AITL)
  - Adult T-cell leukemia/lymphoma (ATLL; acute and lymphoma types only, must be positive for human T cell leukemia virus 1)
  - Enteropathy-associated T-cell lymphoma (EATL)
  - Hepatosplenic T-cell lymphoma
  - Monomorphic epitheliotropic intestinal T-cell lymphoma (MEITCL)
  - Indolent T-cell lymphoproliferative disorder (T-LPD) of the gastrointestinal (GI) tract
  - Follicular T-cell lymphoma
  - Nodal peripheral T-cell lymphoma with T-follicular helper (TFH) phenotype
- Fluorodeoxyglucose (FDG)-avid disease by PET and measurable disease of at least 1.5 cm by CT, as assessed by the site radiologist.

Study Highlights

- International, open-label, multicenter, phase 2 clinical trial designed to evaluate the efficacy and safety of A+CHP in subjects with non-sALCL PTCL and CD30 expression <10% on tumor cells
- Up to approximately 80 subjects will be enrolled in this study.
  - Approximately 40 subjects with positive CD30 expression (≥1% to <10%) and up to approximately 40 subjects with negative CD30 expression (<1%) by local assessment (central confirmation) will be enrolled.
- Efficacy assessments by BICR using Revised Response Criteria for Malignant Lymphoma and modified Lugano criteria
- Safety assessments include surveillance and recording of AEs and concomitant medications, physical examination findings, and laboratory tests
- Approximately 50 sites in United States and Europe
  - United States, United Kingdom, Italy, Spain, France, and Czech Republic
- Enrollment for this global trial is ongoing

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Disclosures

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