ALLELE Study: A Multicenter, Open Label, Phase 3 Study of Tabelecleucel for Solid Organ or Allogeneic Hematopoietic Cell Transplant Subjects with Epstein-Barr Virus-Driven Post-Transplant Lymphoproliferative Disease (EBV+ PTLD) after Failure of Rituximab or Rituximab and Chemotherapy

Poster #283

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BACKGROUND

EBV+ PTLD

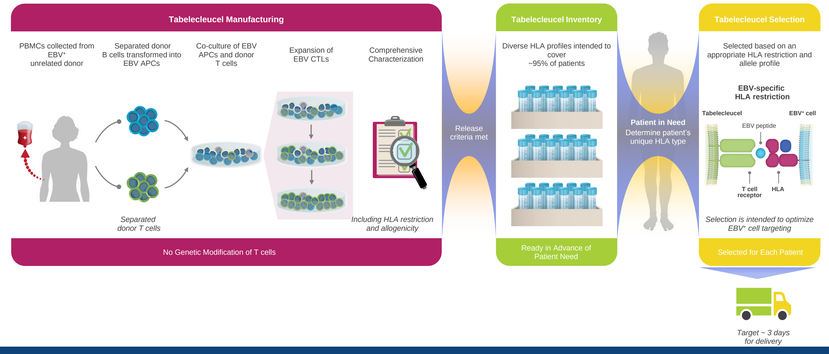
- Epstein-Barr virus-driven post-transplant lymphoproliferative disease (EBV+ PTLD) is a rare and potentially life-threatening complication following solid organ transplant (SOT) or allogeneic hematopoietic cell transplant (HCT) due to compromised T-cell activity by immunosuppression.[1-3]
- Treatment of relapsed/refractory EBV+ PLTD post HCT and SOT is inadequate and has poor overall survival, highlighting a clear unmet medical need. Challenges with current therapies include limited efficacy, potential for graft rejection, or graft-vs-host disease (GvHD), and high mortality.[4-8]
  - A French retrospective study reported a median overall survival (mOS) of < 2 months for 18 patients with EBV+ PTLD post HCT after failure of rituximab ± chemotherapy (CT). 89% of the patients died; of all deaths, 63% were related to PTLD and therapy.[5]
  - In the German PTLD database a mOS of 3.3 months was reported for 36 patients with EBV+ PTLD post SOT after failure of rituximab ± CT. For patients who did not receive CT mOS was less than 2 months from disease progression.[8]

Tabelecleucel

- Tabelecleucel is an off-the-shelf, allogeneic, T-cell immunotherapy selected for each patient from an existing inventory based on an EBV human leukocyte antigen (HLA)- restricting allele and a second shared allele. The manufacturing process is described in **Figure 1**.
- In two phase 2 trials (NCT00002663 and NCT01498484) for EBV+ PTLD patients following HCT or SOT and after failure of rituximab, or rituximab plus CT, treatment with tabelecleucel demonstrated encouraging outcomes.[9]
  - In HCT patients an objective response rate (ORR) of 68% has been elicited. Probability of overall survival at 2 years was 57%.
  - In SOT patients, an ORR of 54% has been elicited. Probability of overall survival at 2 years was 54%.
  - Among responders (HCT and SOT) estimated 2-year OS was 83%.

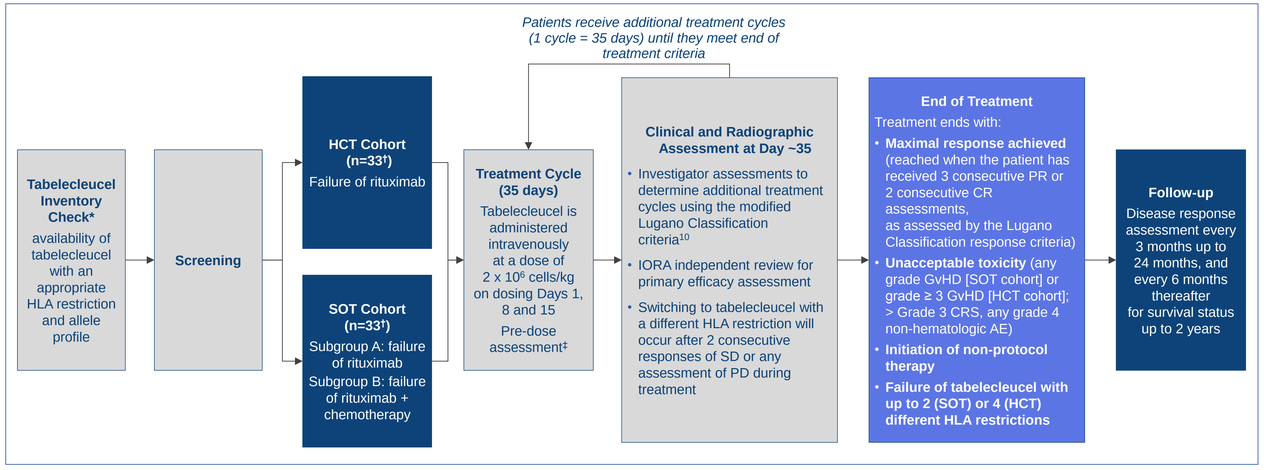
Here, we describe the design of an ongoing phase 3 study (ALLELE; NCT03394365) assessing the efficacy and safety of tabelecleucel for HCT and SOT patients with EBV+ PTLD after failure of rituximab ± CT that recently opened for enrolment in Europe.

Figure 1. Off-the-shelf, Allogeneic Tabelecleucel Manufacturing & Selection Process



STUDY DESIGN

Figure 2. ALLELE Study Design



*Cytomegalovirus serostatus, DNA based high-resolution HLA typing, and patient's weight and demographics.

†Estimated cohort size.

‡Assessments are performed within 7 days before cycle 2 and thereafter and include the following: ECOG status/Lansky score, lactate dehydrogenase, serum EBV DNA, radiographic assessments, hematology, chemistry and anti-HLA antibodies.

AE = adverse event;
CR = complete response;
CRS = cytokine release syndrome;
EBV+ PTLD = Epstein-Barr virus post-transplant lymphoproliferative disease;
ECOG = Eastern Cooperative Oncology Group;
GvHD = graft-versus-host disease;
HCT = hematopoietic stem cell transplant;
HLA = human leukocyte antigen;
IORA = independent oncologic response adjudication;
PD = progressive disease;
PR = partial response;
SD = stable disease;
SOT = solid organ transplant.

ALLELE Endpoints

Primary Endpoint

- ORR – complete response or partial response – obtained following administration of tabelecleucel with up to two different HLA restrictions in the SOT or HCT cohort evaluated by independent oncologic response adjudication (IORA).

Secondary Endpoints

- Duration of response (DOR) in SOT and HCT cohorts separately
- ORR and DOR in SOT and HCT cohorts combined
- Rate of complete response and partial response
- Time to response and time to best response
- Overall survival
- Rates of allograft loss/rejection episodes (for SOT cohort only)

ALLELE Inclusion Criteria

- Prior SOT of kidney, liver, heart, lung, pancreas, small bowel, or any combination of these (SOT cohort); or prior allogeneic HCT (HCT cohort)
- A diagnosis of locally assessed, biopsy-proven EBV+ PTLD
- Confirmation of available appropriate partially HLA-matched and restricted tabelecleucel
- Measurable systemic disease using Lugano Classification by PET/CT
- Treatment failure of rituximab or interchangeable commercially available biosimilar monotherapy (HCT and SOT subgroup A) or rituximab plus any concurrent or sequentially administered chemotherapy regimen (SOT subgroup B) for treatment of PTLD. Treatment failure is defined based on rituximab response as follows:
  - a. Radiographic disease progression per Lugano Classification following a minimum cumulative dose of 1125 mg/m^2 rituximab (typically, 3 weekly doses of 375 mg/m^2), or
  - b. Failure to achieve CR or PR, defined by Lugano radiographic criteria, after a minimum cumulative dose of 1500 mg/m^2 rituximab (typically, 4 weekly doses of 375 mg/m^2), or
  - c. Relapse/progression of PTLD after a response to rituximab (SOT subgroup A or HCT cohort) or rituximab plus chemotherapy (SOT subgroup B), defined as radiographic and/or biopsy evidence of relapse/progression consistent with PTLD; if the underlying disease for which the patient underwent allogeneic HCT (HCT cohort) was lymphoma, biopsy confirmation of relapsed EBV+ PTLD is required
- Males and females of any age
- ECOG performance status ≤3 for patients aged >16 years; Lansky score ≥20 for patients from birth to 16 years
- If allogeneic HCT was performed as treatment for an acute lymphoid or myeloid malignancy, the underlying primary disease for which the patient underwent transplant must be in morphologic remission (HCT cohort only)
- Adequate organ function

ALLELE Exclusion Criteria

- Daily steroids of >0.5 mg/kg prednisone or glucocorticoid equivalent, ongoing methotrexate, or extracorporeal photopheresis
- Untreated CNS PTLD, or CNS PTLD for which the patient is actively receiving treatment
- Grade ≥2 graft-versus-host disease
- Burkitt lymphoma, classical Hodgkin lymphoma, or any T cell lymphoma
- Active adenovirus viremia (HCT cohort only)
- Need for vasopressor or ventilatory support
- Antithymocyte globulin or similar anti-T cell antibody therapy ≤4 weeks prior to enrolment
- Treatment with EBV T cells or CAR T cells directed against B cells within 8 weeks of enrolment (SOT or HCT cohorts); or unselected donor lymphocyte infusion within 8 weeks of enrolment (HCT cohort only)

CAR = chimeric antigen receptor; CNS = central nervous system; CR = complete response; CT = computed tomography; CTL = Cytotoxic T cells; EBV = Epstein-Barr virus; EBV+ PTLD = Epstein-Barr virus post-transplant lymphoproliferative disease; ECOG = Eastern Cooperative Oncology Group; HCT = hematopoietic stem cell transplant; HLA = human leukocyte antigen; mOS = median overall survival; PET = positron emission tomography; PR = partial response; SOT = solid organ transplant.

Now Enrolling in Selected Countries in Europe

For more information about the ALLELE clinical study visit

https://clinicaltrials.gov/ct2/show/NCT03394365

or contact

clinicalstudies@atarabio.com

or visit

https://www.atarabio.com/medical-professionals/

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