Abstract: P1170

Title: PHASE 2 STUDY OF ANTI-PD-L1 ANTIBODY ATEZOLIZUMAB IN PATIENTS WITH RELAPSED/REFRACTORY EXTRANODAL NATURAL KILLER/T-CELL LYMPHOMA: NCCH1903/ATTACK STUDY

Abstract Type: Poster Presentation

Topic: Aggressive Non-Hodgkin lymphoma - Clinical

Background:

Extranodal natural killer/T-cell lymphoma (ENKTL) is a rare lymphoma subtype that is endemic to East Asia. There is an unmet need for patients (pts) with relapsed/refractory (r/r) ENKTL especially for those who failed or are ineligible for asparaginase-containing regimen. Previous studies have suggested the efficacy of immune checkpoint inhibitors (ICIs) targeting programmed cell death-1/programmed cell death ligand-1 (PD-L1) axis on r/r ENKTL. However, no ICIs have achieved regulatory approval for ENKTL in the US, Europe, and Japan.

Aims:

To evaluate the efficacy and safety of anti-PD-L1 antibody, atezolizumab in pts with r/r ENKTL.

Methods:

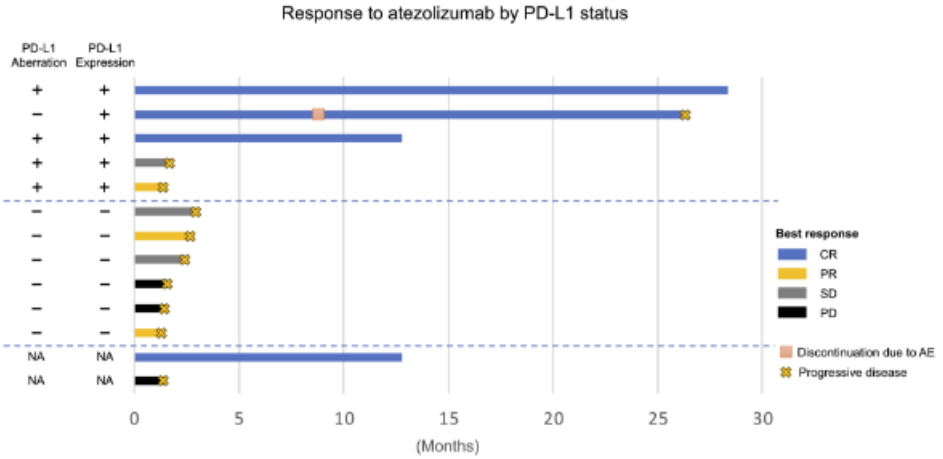
This was a multi-center single-arm phase II study of single-agent atezolizumab (1200 mg, day1, 21-day cycle, up to 2 years, off-label use) in pts with r/r ENKTL (jRCT2031190177). Key eligibility criteria included: histologically confirmed ENKTL, age ≥12, ECOG-PS 0-2, previous history of ≥1 lines of systemic therapy, and having measurable lesion All pts must have history of treatment with SMILE (steroid, methotrexate, ifosfamide, asparaginase, and etoposide) or ineligible to it due to age or comorbidities. Informed consent was obtained before enrollment. Primary endpoint was an independent review committee (IRC)-assessed overall response rate (ORR) based on CT criteria of Lugano classification. Secondary endpoints included complete metabolic response (CMR) rate by PET after Cycle 4, progression-free survival (PFS), overall survival (OS), duration of response (DoR), and safety. Target number of accrual was between 12 to 20 pts and ≥3 responders were required to declare the efficacy of atezolizumab based on our Bayesian design.

Results:

A total of 14 pts were enrolled between Jan-2020 to Sep-2022. In 13 pts for efficacy evaluation after excluding one patient without measurable lesion based on IRC assessment, median age was 72 (IQR 66-77), 6 pts (46.2%) were female, and most pts were PS 1 (n=10, 77%). Three pts (23%) were stage II and 10 pts (77%) were stage IV. B symptoms were present in 6 pts (46%). Plasma Epstein-Barr virus DNA was detectable at baseline in 11 pts (85%). In the safety analysis set (n=14), median number of treatment cycle was 4 (range, 1-35). At the data cut-off (31-Mar-2023), protocol treatment was ongoing in 2 pts, had been completed in 1 pt, and had been discontinued in 11 pts mainly due to progressive disease (n=8) or immune-related adverse events (AEs) (n=2, both had hepatitis grade 3). The IRC-assessed ORR was 54% (7/13) with 4 CRs (31%). The CMR rate after 4 cycles was 23%. With a median follow-up of 24.9 months, the median DoR was not reached. The median PFS was 2.4 months, and the median OS was 10.3 months.

PD-L1 genetic alterations and PD-L1 expression were evaluated by targeted sequencing and immunohistochemistry (IHC) in 11 pts. *PD-L1* genetic alterations were detected in 4 pts (36%), and 3 of 4 pts obtained responses (ORR 75%). Whereas 3 of 7 pts without *PD-L1* alterations achieved responses (ORR 42.9%). PD-L1 expression by IHC was positive in 5 pts (46%), and 4 of 5 pts obtained responses (ORR 80%). The ORR in pts without PD-L1 expression was 33% (2 out of 6). In the safety analysis set, frequently observed AEs in ≥30% were fever (n=9, 64%), neutropenia (n=6, 43%), anemia, leukopenia, and hypoalbuminemia (each n=5, 36%). Two pts experienced grade 3 autoimmune hepatitis but were manageable with steroid and/or mycophenolate mofetil.

Summary/Conclusion: Atezolizumab demonstrated substantial efficacy in pts with r/r ENKTL. *PD-L1* genetic alterations and/or PD-L1 expression by IHC may predict response to atezolizumab.



Keywords: T cell lymphoma, Immunotherapy, Lymphoma therapy