Tislelizumab, a PD-1 inhibitor for relapsed/refractory mature T/NK-cell neoplasms: results from a phase 2 study

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Background: Effective treatment choices for patients (pts) with relapsed/refractory (R/R) mature T/NK-cell neoplasms after failure of standard therapies are limited. Tislelizumab (TIS), a humanized anti-PD-1 mAb, demonstrated outstanding efficacy and favorable safety in pts with R/R classical Hodgkin lymphoma or solid tumors. We present safety and efficacy of the phase 2 study of TIS in pts with R/R mature T/NK-cell neoplasms.

Methods: Pts were enrolled into 3 cohorts stratified by the type of T/NK-cell neoplasm to receive TIS 200 mg intravenously every 3 weeks until disease progression or intolerable toxicity. Eligible pts had ≥1 prior systemic therapy, disease progression during/after most recent therapy completion or refractory disease, ECOG ≤2, and life expectancy ≥6 mo. Primary endpoint was investigator-assessed overall response rate (ORR). Secondary endpoints included duration of response (DoR), complete response (CR) rate, progression-free survival (PFS), overall survival (OS) in cohorts 1 and 2, and safety.

Results: 77 pts were treated. Cohort 1: R/R extranodal NK/T-cell lymphoma (n=22); cohort 2: R/R mature T-cell neoplasms (n=44; 21 peripheral T-cell lymphoma not otherwise specified; 11 angioimmunoblastic T-cell lymphoma; 12 anaplastic large cell lymphoma); cohort 3: R/R cutaneous T-cell lymphomas (CTCL; stage ≥1B; n=11; 8 mycosis fungoides and 3 Sézary syndrome). Of all pts, 76.6% had advanced-stage disease, 51.9% had refractory disease, and 49.4% had ≥3 prior systemic regimens. Median treatment cycles for cohorts 1, 2, and 3 were 5 (range, 1-37), 4.5 (range, 1-38), and 17 (range, 3-25), respectively. Cohort 3 had promising efficacy (median follow-up [FU] 16.6 mo): ORR 45.5%; CR 9.1%; median DoR 11.3 mo (95% CI: 2.76-11.30); median PFS 16.8 mo; median OS not reached (NR). Modest efficacy was reported in cohort 1 (median FU 8.4 mo): ORR 31.8%; CR 18.2%; median DoR NR (95% CI: 2.66-not estimable [NE]); median PFS 2.7 mo; median OS 8.8 mo and also in cohort 2 (median FU 9.3 mo): ORR 20.5%; CR 9.1%; median DoR 8.2 mo (95% CI: 2.50-NE); median PFS 2.7 mo; median OS 13.3 mo. Most frequent adverse events (AEs) were pyrexia (32.5%), anemia (18.2%), arthralgia (18.2%), and diarrhea (15.6%); most frequent grade ≥3 AEs were anemia (7.8%), pneumonia (6.5%), and neutropenia (5.2%). Any grade immune-mediated AEs occurred in 22 (28.6%) pts, most frequently hypothyroidism (10.4%), hyperglycemia (5.2%), and rash (5.2%); and grade ≥3 in 4 (5.2%) pts (blood creatine

phosphokinase increased, hepatitis, hypothyroidism, rash, and urticaria [1 pt each]). No treatment-related AEs led to death.

Conclusions: TIS was well tolerated, achieving modest efficacy in R/R mature T/NK-cell neoplasms, with some long-lasting remissions particularly in CTCL. Further studies are warranted to determine the biologic features associated with response and explore optimal combination therapies.