INTRA- AND INTER-PATIENT COMPARISON OF EFFICACY BETWEEN TWO PHASE II STUDIES OF TRABECTEDIN (T) IN PATIENTS (PTS) WITH TRANSLOCATION-RELATED SARCOMAS (TRS): A RANDOMIZED COMPARATIVE STUDY (STUDY-C) AND A SINGLE ARM STUDY (STUDY-S)


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Aim: T binds to the minor groove of DNA and blocks DNA repair machinery. In addition, T inhibits interactions of transcription factors with DNA. It has been reported that T is an active drug in TRS pts unresponsive to available chemotherapies with a significant increase in progression-free survival (PFS) and overall survival in study-C (ASCO 2014, Abstract: 10524). For pts with confirmed disease progression in best supportive care (BSC) arm of study-C, study-S as a rescue therapy was conducted to evaluate safety and efficacy of T. Efficacy for pts who were enrolled in both studies and efficacy difference for T between study-C and study-S were evaluated.

Methods: Target population of study-C was pts with histologically proven TRS of 14 types and unresponsive or intolerable to standard chemotherapy. After confirmation of disease progression based on image assessments in study-C, pts who were assigned to BSC were enrolled in study-S if they signed a consent form. Pts received T as a 24-hour continuous infusion every 21 days. We analyzed intra-patient comparison between BSC in study-C (BSC/C) and T in study-S (T/S), and inter-patient comparison between T in study-C (T/C) and T/S. We used a multivariate Cox proportional hazard model adjusted by background factors to estimate hazard ratios (HRs) for PFS in these comparisons.

Results: In study-C, 76 pts were randomized: 39 in T and 37 in BSC arm. Out of 37 pts in BSC arm of study-C, 31 pts were enrolled in study-S. Number of pts for efficacy analysis of T/C, BSC/C and T/S were 37, 29 and 29 respectively. Median PFS (95% confidence interval) for T/C, BSC/C and T/S were 5.6 month (4.1-7.5), 0.9 month (0.9-1.0), and 7.3 month (2.9-9.1), respectively. HRs for PFS in intra- (BSC/C vs T/S) and inter-patient (T/C vs T/S) comparison were 0.08 (P<0.0001) and 1.03 (P=0.9390), respectively.

Conclusions: PFS was significantly prolonged in T/S compared with BSC/C, and was not different between T/C and T/S. Although contribution to survival is not evaluated, it is expected T could suppress progress of advanced TRS even at the late stage.

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