Stopping tyrosine kinase inhibitor in chronic myeloid leukemia; perspectives from Korean data

Hawk Kim

Gachon University College of Medicine, Korea

The objectives of treating chronic myeloid leukemia (CML) have changed from the prolonging overall survival by achieving adequate cytogenetic/molecular responses to treatment free remission (TFR) which became of the new therapeutic target by European LeukemiaNet 2017 recommendation. There are many clinical trials for TFR in CML patients taking second generation tyrosine kinase inhibitors (TKIs) as well as imatinib.

Early Korean retrospective data in 2012 for stopping imatinib analyzed 14 patients defining TFR as maintenance of complete molecular response (CMR; currently molecularly undetectable leukemia [MUL]). The overall probability of persistence of CMR at 1 year was 28.6% (95% Confidence Interval [CI], 16.5–40.7). The duration of IM therapy after achieving a CMR showed a marginally significant trends for overall probability for CMR persistence (P = 0.076). Long-term follow up retrospective multicenter data were published in 2016. The criterion of TFR was the undetectable minimal residual disease (UMRD) persistence. Nineteen patients were enrolled and the estimated UMRD persistence rate at 5 years was 23.7% (95% CI 13.2–34.2). The rate of UMRD persistence at 5 years was significantly lower in patients with a high- risk Sokal score at diagnosis than in those with low- to intermediate-risk Sokal scores (0 vs. 40.9%, $p < 0.001$).

The first prospective TFR study in Korea was Korean imatinib stop study (KIDS) published in 2013. KIDS study defined TFR failure as 2 consecutive losses of major molecular response (MMR). The TFR rate was the overall 12- month and 24-month probability of sustained MMR was 62.2% and 58.5%, respectively. Follow up data of KIDS showed

The Korean Society of Hematology Chronic Myeloid Leukemia Working Party (CMLWP) conducted a retrospective TFR study was ASTER study that enrolled 93 patients. TFR at 5 years was 47.9 % and 44.4 %, for MR3.0 loss and UMRD loss, respectively. A prospective multicenter study of TFR (Digital CML study) was conducted by CMLWP. The study was closed after enrolling total 78 patients. After TKI discontinuation, digital polymerase chain reaction (dPCR) was measured at regular intervals to check the relationship between changes in BCR/ABL1 levels and molecular recurrence survival, and to select a patient group that can safely discontinue TKI.

New prospective TFR studies of CMLWP are ASTER-P as a first TFR trial and ASTER-A as a second TFR trial. CMLWP will publish a new Korean guideline for CML treatment and TFR in consideration of these Korean data.