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Clinical Oncology 2018: Current treatment option of Chronic Myeloid Leukemia (CML): Focusing on Radotinib - Young Rok Do - Keimyung University School of Medicine, Korea

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Background: Radotinib is a second-generation BCR-ABL1 tyrosine kinase inhibitor (TKI) approved in Korea for CML-CP in patients newly diagnosed or with insufficient response to other TKIs. This study called RERISE study (NCT01511289) was conducted to evaluate the efficacy and safety of radotinib as first-line therapy for CML-CP. In RERISE phase 3 studies, radotinib demonstrated significantly higher and faster rates of major molecular response (MMR) than imatinib in patients with newly diagnosed CML-CP. By 12 and 24 months follow up, MMR (BCRABL1IS ≤ 0.1%) and MR4.5 (BCR-ABL1IS ≤ 0.0032%) in radotinib 300 mg twice daily (BID) were higher than imatinib group. Also, early molecular response (EMR) at 3- or 6- months could predict better outcomes in both radotinib or imatinib groups. To confirm the long-term benefits and risks of radotinib 300mg bid and imatinib 400mg qd, we update the results from RERISE phase 3 study based on a minimum follow-up of 36 months.

Methods: This multinational, open-label study assigned patients (1:1:1) to one of two bid radotinib doses, or imatinib qd. The primary endpoint was MMR by 12 months. 241 patients were randomized 1:1:1 to radotinib 300 mg bid (n=79), radotinib 400 mg bid (n=81), or imatinib 400 mg qd (n=81). Methods have been previously reported (Blood 2015 126:476). We evaluated MMR and MR4.5, overall survival (OS), and progression-free survival (PFS) by 36 months. Also, we analyzed the clinical impacts of early and deeper molecular response in radotinib 300mg bid and imatinib 400 mg qd groups.

Results: By 36 months, MMR was significantly higher in patients receiving radotinib 300 mg bid compared with imatinib 400mg qd. The MR4.5 rate by 36 months was also higher for radotinib compared to imatinib (43% vs. 28%; P=0.0538). More patients treated with radotinib achieved additional MMR and MR4.5 since 12 months and time to MR4.5 was faster in radotinib than imatinib (median 924 vs. 1,095 days; P=0.2534). Of 59 patients who had MMR by 36 months, 18 patients achieved MMR, and of 34 patients who had MR4.5 by 36 months, 22 patients achieved MR4.5 since 12 months. Estimated OS and PFS rate at 36 months were not significantly different in two groups (99% vs. 98%; P=0.6204, 99% vs. 96%; P=0.3070). Treatment failure was lower in radotinib group compared with imatinib group (Table). The safety profiles were consistent with those previously reported and most of adverse events (AEs) have developed within 12 months. Since 12 months, newly developed AEs such as rash, nausea/vomiting, pruritis, musculoskeletal pain, fatigue, hyperbilirubinemia, and ALT elevation, etc. have shown minimal increase by 36 months FU.

Conclusions: With a minimum 36 months follow-up, radotinib continued to demonstrate significantly higher rates of MMR and MR4.5 than imatinib in newly diagnosed CML-CP. Also, these responses with radotinib were earlier and deeper compared with imatinib. These results still demonstrate that radotinib can be one of the standards of care in newly diagnosed CML-CP and support the higher possibility of treatment-free remission (TFR) on frontline therapy with radotinib.

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