KSN 2016 Abstract Submission

Clinical Nephrology

KSN2016ABS-1348

The oral intestinal sorbent AST-120 favorably affects renal and cardiovascular outcomes in patients with advanced renal dysfunction: subgroup analysis of K-STAR study

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Background: Kremezin Study Against Renal disease progression in Korea (K-STAR) study evaluated the long-term effect of AST-120 on the renal disease progression. Primary analysis did not show positive effect of AST-120. We aimed to find good candidates for the AST-120 prescription through subgroup analysis.

Methods: Patients in the AST-120 arm were given six gram of AST-120 in three divided doses per day, and those in the control arm received only standard conventional treatment (open label design) for 36 months or until the occurrence of primary outcomes. We evaluated 465 per-protocol group patients who completed the study without withdrawal or drop-out. Primary outcome was composite of doubling of serum creatinine (SCr), estimated glomerular filtration rate (eGFR) decrease more than 50%, or initiation of renal replacement therapy.

Results: There was not a significant difference in change in uremic toxins in the AST-120 and control arm. Two arms were not different in the occurrence of composite primary outcomes [97 events in 226 individuals in the AST-120 arm, 97 events in 239 individuals in the control arm, HR 1.15 (95% CI 0.87-1.53)] (log-rank P = 0.33). The change in proteinuria was similar in the two treatment arms over time. There was not a difference in mortality (9 AST-120, 11 control, log-rank P = 0.80) or unplanned hospitalizations (93 AST-120, 102 control, log-rank P = 0.91) in the two treatment arms. There was no significant difference of the health-related QOL score between two arms. But the slope of 1/ SCr was slower in the AST-120 arm than control arm (P = 0.046). The decline in eGFR was slower in patients with diabetic nephropathy ($P_{randomization-time}$ = 0.049) and in patients without primary outcomes (P = 0.01). When we calculated the ratio of serum indoxyl sulfate (IS) level one year after AST-120 treat to the level at the time of randomization and divided it to tertile groups, the amount of daily proteinuria one year after the randomization was lower in the lowest tertile group than those

of other two groups (P = 0.038). And the cumulative rate of composite primary outcomes was significantly lower in the lowest tertile group than the others in a row (Log-rank P = 0.033) [intermediate tertile HR 1.852 (95% CI 0.982-3.492), P = 0.057; highest tertile HR 1.915 (95% CI 1.011-3.626), P = 0.046]. And the AST-120 arm showed less major adverse cardiovascular outcomes than the control arm (HR 0.51 (95% CI 0.26-0.99), P = 0.046).
Conclusion: Long-term use of AST-120 added to standard treatment showed more preserved renal function, especially in patients with diabetic nephropaty, and less slope of 1/SCr. And the magnitude of serum IS decrement over 1 year by AST-120 showed reverse correlation with the occurrence of primary outcome. In addition, AST-120 group showed less cardiovascular events. We need another study to verify that compliant and longer duration of AST-120 medication ameliorates the renal progression.

Keywords: Advanced renal dysfunction, AST-120, Treatment outcome