

Future plan for global Phase III clinical study of ART-123

Asahi Kasei Pharma has determined its future plan regarding global Phase III clinical study of ART-123 (generic name: thrombomodulin alfa; marketed as Recomodulin™ in Japan) being developed by its subsidiary Asahi Kasei Pharma America Corp. for the treatment of severe sepsis with coagulopathy.

Asahi Kasei Pharma has elucidated the following points^{1), 2)} through further analysis of data from the completed global Phase III clinical study performed thus far (SCARLET study; n=800).

1. A statistically significant difference was not observed in the primary endpoint of 28-day all-cause mortality compared to the placebo control group. Whereas 28-day all-cause mortality for the group given ART-123 was 26.8% (106 of 395 cases), that for the control group was 29.4% (119 of 405 cases), the difference being 2.55%. However, among patients whose coagulopathy continued until just before study drug administration (n=634; PT-INR* > 1.4 and platelet count > 30,000/mm³) a 5.40% difference in 28-day all-cause mortality (26.7% (82/307) for the group given ART-123 and 32.1% (105/327) for the control group) was observed.
2. Upon confirmation of correlation between the concentration of blood coagulation markers thrombin-antithrombin complex and prothrombin fragment F1+2 just before study drug administration and 28-day all-cause mortality of the group given ART-123 and the control group, it was found that mortality for the group given ART-123 was lower than that for the control group when these parameters were above the upper limit of their normal ranges, especially when these parameters were higher than or equal to their median values of the entire population. This suggests that among patients with coagulopathy, mortality for the group given ART-123 may be lower than that for the control group, and supports the analytical result described in 1., above.

Based on such data from the SCARLET study, Asahi Kasei Pharma has discussed the design of the next study with the United States Food and Drug Administration (FDA), and reached agreement concerning a study design which newly includes reconfirmation of coagulopathy at a timing near study drug administration. In consideration of this discussion with the FDA, Asahi Kasei Pharma has decided to discontinue the second global Phase III clinical study (SCARLET-2) registered on the ClinicalTrials.gov database of clinical studies and, after amending the study design, proceed with development for the said indication while seeking opportunity for co-development and/or out-licensing.

Note that subjects of the SCARLET study were patients with sepsis-associated cardiovascular dysfunction or respiratory dysfunction, and coagulopathy (PT-INR > 1.4 and platelet count greater than 30,000/mm³ but less than 150,000/mm³ or decreasing by over 30% within 24 hours). The intended indication of the development, severe sepsis with coagulopathy, differs from the approved indication for ART-123 in Japan, disseminated intravascular coagulation (DIC).

Asahi Kasei Pharma will continue to report results of the SCARLET study through presentations at scientific conferences and the publication of scientific papers.

* Prothrombin time–international normalized ratio.

¹⁾ JL Vincent et al, JAMA 2019, 321(20), 1993-2002

²⁾ D Fineberg et al, presentation at ISTH 2019