Category :**Hematology: bleeding\transfusion**

A283 - ***A phase 3, randomized, double-blinded study of four-factor prothrombin complex concentrate in patients with acute major bleeding on direct oral anticoagulant therapy with factor xa inhibitors: the lex-210 study***

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Introduction:

LEX-210 aims to demonstrate hemostatic efficacy/safety of four-factor prothrombin complex concentrate (4F-PCC; *Octaplex*®, Octapharma) in adults with acute major bleeding on direct oral anticoagulant (DOAC) therapy with Factor Xa Inhibitors (FXaI). Patients on FXaI can experience major bleeding associated with substantial morbidity, mortality, and hospitalization. Therefore, reversal/hemostatic agents are used to control FXaI-related bleeding. The efficacy/safety of PCCs as hemostatic agents for FXaI-related bleeding requires further investigation.

Methods:

LEX-210 (NCT04867837) is a Phase 3, multicenter, prospective, randomized, double-blinded, group-sequential, parallel-group, adaptive design study. Key inclusion criteria include major bleeding and DOAC level ≥100 ng/ml equivalent; exclusion criteria include life-threatening bleeding and acute trauma for which hemostatic agent alone would not control bleeding. LEX-210 will enroll ~200 patients, randomized 1:1 to receive 50 IU/kg or 15 IU/kg 4F-PCC to demonstrate superior hemostatic efficacy of high dose 4F-PCC for emergent FXaI-related major bleeding. The primary endpoint is the proportion of patients with effective (excellent/good rating) or non-effective (poor/none rating) hemostasis in bleeding management within 24 h of 4F-PCC, as assessed by an independent adjudication committee according to predefined criteria (**Figure-1**) [1]. Secondary endpoints include changes in endogenous thrombin potential; 30-day rate of thromboembolic events, all-cause mortality and adverse events; vital signs; and laboratory parameters.

Results:

LEX-210 commenced in Q4 2021 and will be performed at ~60 sites in North America and Europe. Completion is expected Q1 2024.

Conclusion:

If results confirm 4F-PCC hemostatic efficacy/safety in the management of FXaI-related major bleeding, it would offer an alternative for the management of major bleeding in these patients.

References:

Sarode R et al. Circulation 128:1234-43, 2013

Image :

Table 1. Hemostatic effectiveness assessment criteria by bleeding type.

Hemostatic Effectiveness Outcome	Hemostatic Effectiveness Assessment Criteria [1]	
	Visible Bleeding	**Non-visible Bleeding**
Excellent (Effective)	Cessation of bleeding ≤1 hour after the end of infusion and no additional coagulation intervention (plasma, whole blood products not including pRBCs, and/or coagulation factors) required	**1.** Musculoskeletal bleeding: pain and swelling are stable or reduced or unequivocal improvement in objective signs of bleeding ≤1 hour after the end of infusion; and the condition has not deteriorated during the 24-hour period **2.** ICH: ≤20% increase in hematoma volume[1] compared to baseline on repeat CT scan performed at the 12-hour time point **3.** Non-visible bleeding that is not described above (e.g., GI bleeding): ≤10% decrease in both Hb/Hct[2] at 24 hours[3] compared to baseline (initial correction of decrease in Hb with pRBC, with a transfusion trigger of a Hb ≤8 ± 1 g/dL [i.e., transfuse pRBC if the Hb ≤8 ± 1 g/dL])
Good (Effective)	Cessation of bleeding >1 and ≤4 hours after end of infusion and no additional coagulation intervention (plasma, whole blood products not including pRBC, and/or coagulation factors) required	**1.** Musculoskeletal bleeding: pain and swelling are stable or reduced or unequivocal improvement in objective signs of bleeding >1 and ≤4 hours after the end of infusion; and the condition has not deteriorated during the 24-hour period **2.** ICH: >20%, but ≤35% increase in hematoma volume[1] compared to baseline on a repeat CT scan performed at the 12-hour time point **3.** Non-visible bleeding that is not described above: >10 to ≤20% decrease in both Hgb/Hct[2] at 24 hours[3] compared with baseline (initial correction of decrease in Hgb with pRBC, with a transfusion trigger of a Hgb ≤8 ± 1 g/dL [i.e., transfuse pRBC if the Hgb ≤8 ± 1 g/dL])
Poor/None (Non-effective)	Cessation of bleeding >4 hours after end of the infusion, and/or additional coagulation intervention (plasma, whole blood products not including pRBC, and/or coagulation factors) required	**1.** Musculoskeletal bleeding: pain is not controlled or swelling is increased by 4 hours after the end of infusion or the condition has deteriorated during the 24-hour period **2.** ICH: >35% increase in hematoma volume[1] compared to baseline on repeat CT scan performed at the 12-hour time point **3.** Non-visible bleeding that is not listed above: >20% decrease in both Hgb/Hct[2] at 24 hours[3] compared to baseline (initial correction of decrease in Hgb with pRBC, with a transfusion trigger of a Hgb ≤8 ± 1 g/dL [i.e., transfuse pRBC if the Hgb ≤8 ± 1 g/dL])

[1] Use maximum thickness in case volume cannot be measured for subarachnoid bleed and subdural hematoma
[2] The smallest percentage decrease in Hb or Hct should be used to determine the hemostatic efficacy rating of excellent, good or poor/none.
[3] Assumption for the 24-hour adjusted Hb/Hct calculation: for each unit of pRBC transfusion there is generally an increase of 1 g/dL in Hb or 3% increase in Hct.

Criteria modified from Sarode R *et al.*, 2013 [1].

Fig -1