

Four-Factor Prothrombin Complex Concentrate (4F-PCC) Versus Plasma for Patients Undergoing Urgent Surgery or Invasive Procedure

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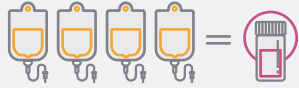
HIGHLIGHTS

4F-PCC

demonstrated noninferiority and superiority to plasma for rapid INR reversal and effective hemostasis



There was **no evidence of an increased risk of thromboembolic complications** for 4F-PCC compared with plasma



Patients at higher risk of volume overload who need VKA reversal **may benefit from treatment with 4F-PCC or plasma**

INTRODUCTION

4F-PCC or plasma

are rapid VKA-reversal options for patients needing urgent surgical or invasive procedures

To minimize the risk of peri-procedural bleeding in patients needing urgent surgical or invasive procedures, **rapid reversal of VKA-induced anticoagulation is often needed**

STUDY CHARACTERISTICS

Objective

4F-PCC compared with plasma for urgent VKA reversal

Study design

Multicenter, open-label, Phase 3b randomized trial

Patient population

≥18 years of age

Endpoints

Primary

Effective hemostasis (intention-to-treat efficacy [ITT-E])

Coprimary endpoint

Rapid INR reduction (INR ≤1.3 at 0.5 h post-infusion)

Secondary (prespecified) endpoints

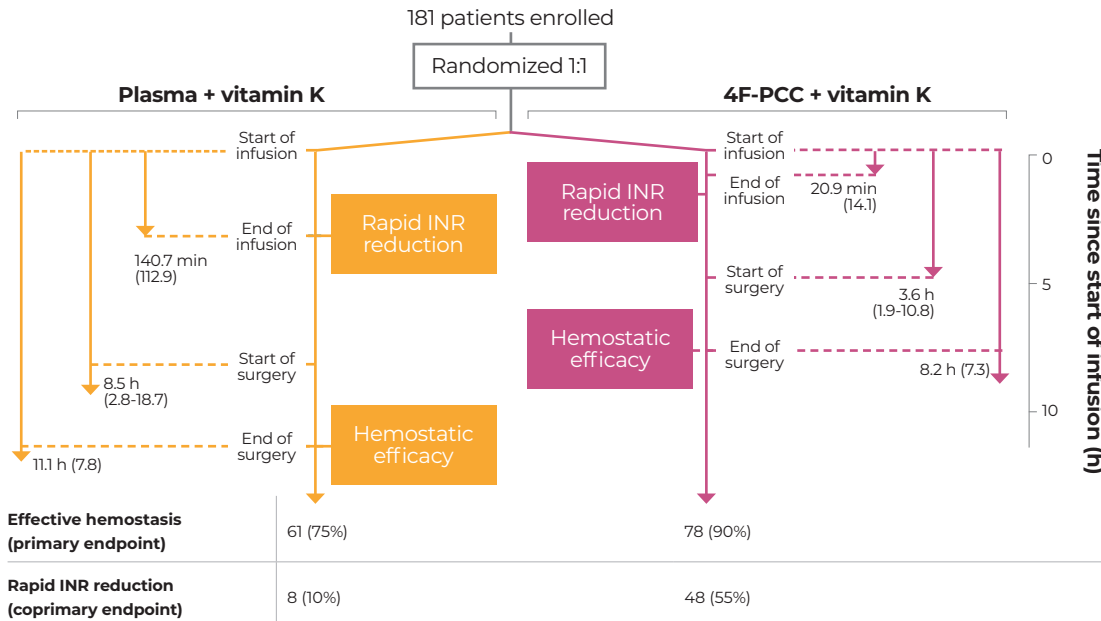
Time to INR reduction (INR ≤1.3) from start of infusion

Safety

Serious adverse safety events (thromboembolic events, fluid overload, rebleeding, deaths)

RESULTS

Figure 1. Study overview (ITT-E population*)

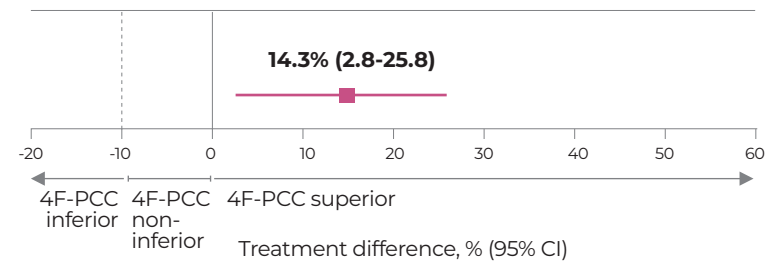


*168 patients were included in the ITT-E population (87 in the 4F-PCC group and 81 in the plasma group). 28 patients (13 receiving 4F-PCC and 15 receiving plasma) who needed nonsurgical invasive procedures were enrolled in the study.

Figure 2. Primary and coprimary endpoints

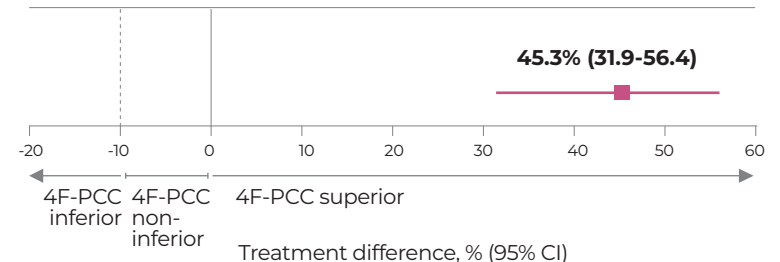
Effective hemostasis (primary endpoint)

P=0.0142



Rapid INR reduction (coprimary endpoint)

P<0.0001



RESULTS

Time to surgery



Median time to surgery in 4F-PCC group was **~5 hours faster**



INR of ≤ 1.3 achievement was **more rapid with 4F-PCC**



54% of 4F-PCC-treated patients had an INR of ≤ 1.3 (1 h post-infusion)

Figure 3. Secondary endpoint: INR correction in the ITT-E population

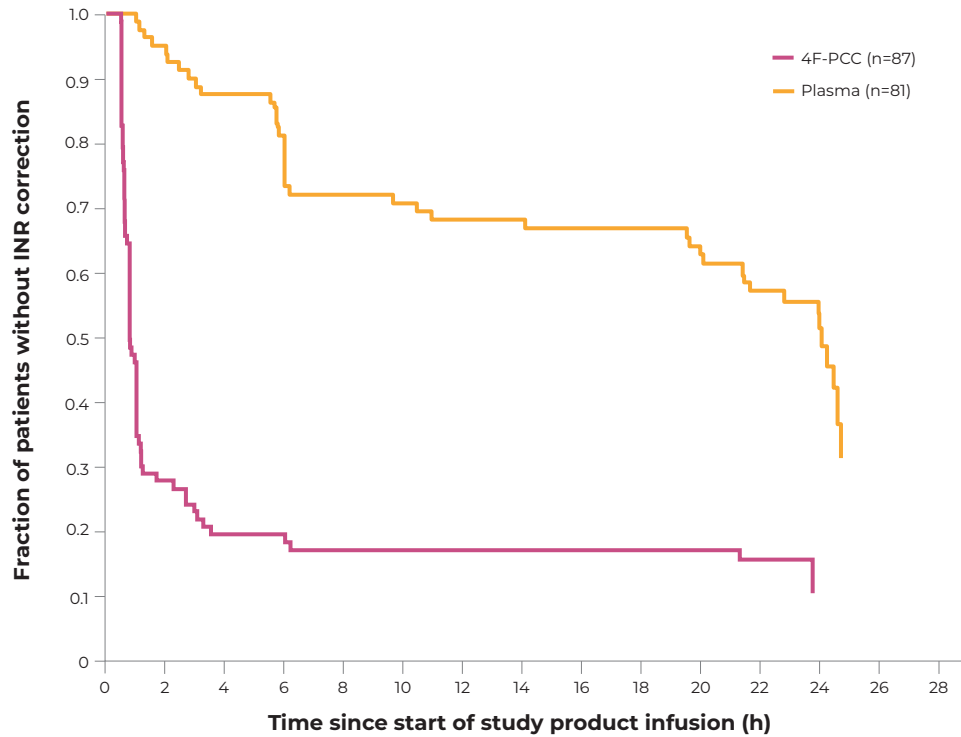
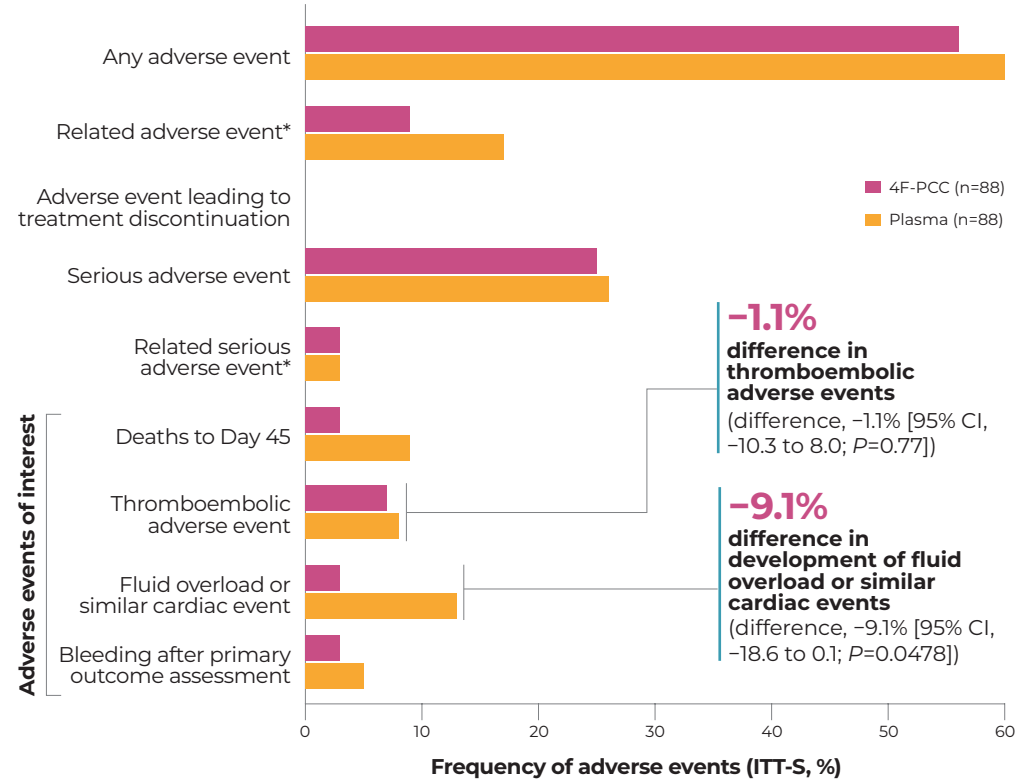


Figure 4. Safety comparisons: Adverse events in the ITT-S population

The frequency of adverse events and serious adverse events, including those related to treatment, was comparable between both groups.



Adverse events with missing treatment associations were classified as related to treatment.
*Defined as events that were related to study treatment according to the investigator.

Abbreviations

4F-PCC: four-factor prothrombin complex concentrate; INR: international normalized ratio; ITT-E: intention-to-treat efficacy; ITT-S: intention-to-treat safety; VKA: vitamin K antagonist.

Reference

Goldstein JN, Refaai MA, Milling TJ Jr, et al. *Lancet*. 2015;385(9982):2077-2087.



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