FRESENIUS KABI

Safety and efficacy of 6 % Hydroxyethyl Starch (HES) in patients undergoing major surgery: **The Randomised Controlled PHOENICS trial**

Key question

Is the perioperative use of HES non-inferior to crystalloids in terms of acute kidney injury?

Setting

53 study sites in
10 European countries

Population

Patients undergoing elective abdominal surgery:
Expected blood loss **≥ 500 mL**
Age: **40 - 85 years**
ASA status: **II-III**

Intervention

6 % HES 130/0,4 (n=977) or crystalloid solution (n=981) given intraoperatively at a maximum dose of 30 mL/kg up to 24 h afterwards.

Study design & duration

PHOENICS is the largest prospective, randomised, controlled, double-blind study of HES vs. crystalloid in major surgery. Main duration was 90 days after surgery. Follow-up call took place 1 year post treatment.

Conclusion

PHOENICS provides robust evidence that perioperative in-label use of HES is well tolerated. Haemodynamic stabilisation showed favourable results for HES.

Endpoints:

Primary:

Primary endpoint of early postoperative renal function, measured as Cystatin-C based eGFR: HES was non-inferior (refer to Fig 1)

Secondary:

Secondary endpoint of mortality and major post-operative complications (including renal) at 90 days: HES was non-inferior

Summary

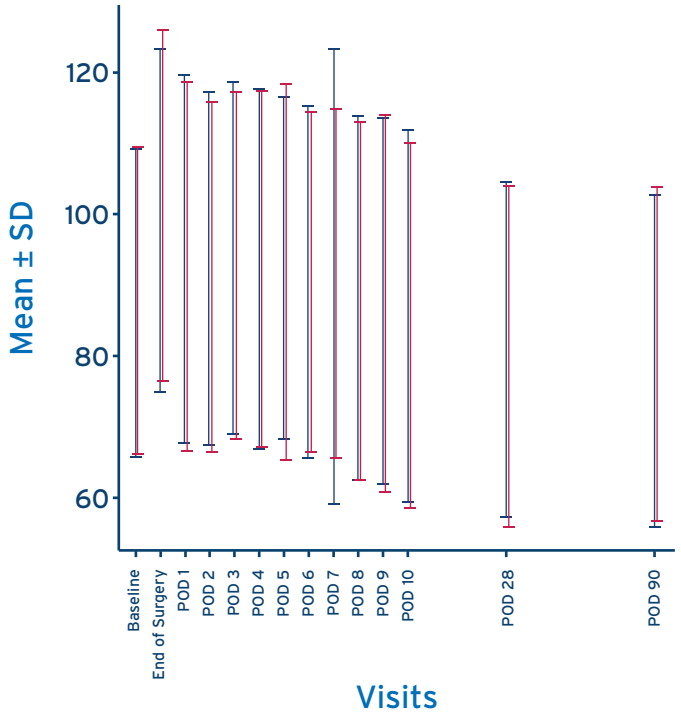
1. Similar safety profiles of both treatments, lower incidence for serious renal adverse events & for AKI (Acute Kidney Injury) for Volulyte group

2. More efficacious:
   - Significantly lower volume of Volulyte needed for haemodynamic stabilisation:
     - **Mean (SD) 616,8 vs 1 155,7 (p = 0,0002)**
   - Net fluid balance was significantly less in Volulyte group:
     - **2 899,9 mL vs 2 693,6 mL**

3. Better haemodynamic stabilisation:
   - Significant difference in change of MAP (Mean Arterial Pressure) from baseline
   - Significantly less need for vasoactive/inotropic drugs **(26 % vs 35 % p < 0,0001)**

4. Similar blood loss between both groups (approx. **0,8 L**) indicating that the use of Volulyte does not increase intraoperative bleeding risk

Cystatin-C based eGFR (mL/min/m²) over time



Treatment:

HES

Crystalloid

Postoperative Day (POD)

Fig 1: Cystatin-C based eGFR over time (Adapted from Buhre et al, 2025)

Why a non-inferiority study vs a crystalloid?

1. **Crystalloids Are the Standard of Care**

   Crystalloids (like saline or balanced electrolyte solutions) are the most commonly used and widely accepted fluids for perioperative volume replacement. They are considered the reference (control) treatment for safety and efficacy in most guidelines.

2. **The regulatory authority in the EU (European Medicines Agency) required robust evidence that HES is not inferior to crystalloids in surgical patients, especially regarding kidney safety and major complications.**

3. **Proving Non-Inferiority or Safety**

   - By comparing HES to crystalloids, researchers can directly assess whether HES is as safe as the current standard.
   - If HES shows no increase in adverse outcomes (e.g., AKI, bleeding, mortality) compared to crystalloids, it supports the safe use of HES in the studied population.

4. **Clinical Relevance**

   - Surgeons and anaesthesiologists need to know if using HES offers any advantage or poses any additional risk compared to what they already use (crystalloids).
   - A direct comparison provides practical, actionable evidence for clinical decision-making

References

1) Buhre W, et al. Safety and efficacy of 6% hydroxyethyl starch in patients undergoing major surgery: The randomised controlled PHOENICS trial. Eur J Anaesthesiol 2025;42:1-10.

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