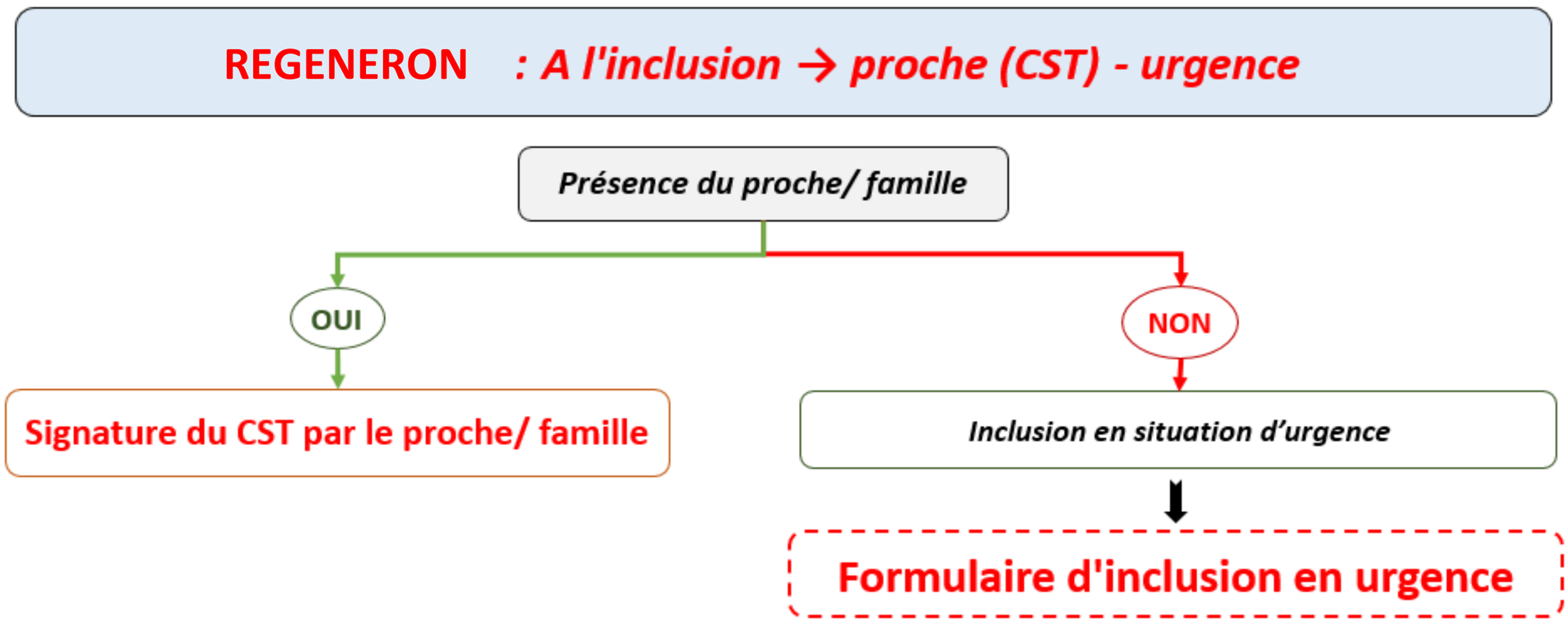
<u>REGENERON :</u> Phase 2, multicenter, randomized, double-blind, placebo-controlled, parallel group, POC study of a single IV dose of REGN7544 in participants with sepsis-induced hypotension who are receiving SOC therapy.



CRITERES D'INCLUSION

1. Patients entre 18 et 85 ans.
2. Infection prouvée ou suspectée, définie par l'administration ou la planification d'une antibiothérapie pendant la période de screening.
3. Hypotension induite par le sepsis ne répondant pas aux fluides IV (≥ 20 ml/kg de cristalloïdes), sous 1 ou 2 vasopresseurs à une dose d'au moins 0,2 µg/kg/min NAD, avec une PAM ≥ 65 mmHg (cible : 65-75 mmHg) pendant au moins 2 heures consécutives avant la randomisation.
4. Critères à remplir pendant 2 heures consécutives avant la randomisation :
   - PAM ≥ 65 mmHg, cible 65-75 mmHg
   - 1 ou 2 vasopresseurs, dose combinée entre 0,1 et 1,0 µg/kg/min NED
   - Pas de changement du nombre de vasopresseurs

CRITERES D'EXCLUSION

1. Unable to obtain informed consent by participant or LAR (according to country- and IRB/EC-specific regulations).
2. Unwilling or unable to comply with clinic visits and study-related procedures.
3. Clinical status requires vasopressor and/or BP management inconsistent with the study protocol
4. Anticipated to discontinue vasopressors within 48 hours of randomization in the opinion of the investigator
5. **Planned procedure (eg, surgery) within 24 hours of randomization.**
6. **Receiving continuous neuromuscular blockade** during the screening period.
7. Primary cause of hypotension suspected to be due to non-sepsis cause (eg, hemorrhage, burns, or cardiogenic shock), including shock after cardiac arrest.
8. **Ejection fraction <20%** in the most recent known echocardiogram.
9. **Acute coronary syndrome based on clinical symptoms and/or ECG during hospitalization** (eg, ST elevation myocardial infarction).
10. History of hospitalization due to heart failure, myocardial infarction, stroke, clinically significant ventricular arrhythmia (eg, sustained VT requiring medication adjustments or cardioversion), transient ischemic attack, or unstable angina within the preceding 3 months
11. Any prior diagnosis of severe pulmonary hypertension meeting one or more of the following criteria:
    a. Echocardiographic evidence of more than moderate pulmonary hypertension, defined as an estimated right ventricular systolic pressure ≥55 mm Hg on the most recent echocardiogram prior to or during the screening period, or
    b. Severe right ventricular dilation/hypertrophy or flattening of the interventricular septum consistent with severe pulmonary hypertension on the most recent echocardiogram prior to or during the screening period, or
    c. Mean pulmonary artery pressure >40 mm Hg by right heart catheterization within the past year, if available.
12. Receiving 3 or more vasopressors, during the screening period or at the time of study drug administration
13. Combined vasopressor dose exceeds 2 µg/kg/min NED during the screening period or at the time of study drug infusion
14. **Cirrhosis with Child-Pugh Score ≥10** or acute hepatic failure with MELD score of ≥30.
15. **On ECMO** or other extracorporeal therapy during the screening period or at the time of study drug adminiastration
16. **Expected death within 24 hours.**
17. **Chronic mechanical ventilation for any reason** or severe chronic obstructive pulmonary disease (COPD) requiring either continuous daily oxygen use or mechanical ventilation (for acute exacerbation of COPD) prior to hospital admission.
18. Received bone marrow transplant during the preceding 6 months or chemotherapy during the preceding 30 days for lymphoma or leukemia.
19. Known allergy or hypersensitivity to components of the study drug.
20. Prior enrollment in this study.
21. **Decision to limit full care taken before obtaining informed consent** (eg, do not resuscitate, do not intubate)
22. Members of the clinical site study team and/or their immediate family unless prior approval granted by the sponsor.
23. Pregnant or breastfeeding women.
24. Women of childbearing potential (WOCBP)* who are unwilling to practice highly effective contraception for at least 90 days following study drug administration. Highly effective contraceptive measures include:
    a. Stable use of combined (estrogen and progestogen containing) hormonal contraception (oral, intravaginal, transdermal) or progestogen-only hormonal contraception (oral, injectable, implantable) associated with inhibition of ovulation initiated 2 or more menstrual cycles prior to screening;
    b. Intrauterine device; intrauterine hormone-releasing system;
    c. Bilateral tubal occlusion/ligation;
    d. Vasectomized partner (provided that the male vasectomized partner is the sole sexual partner of the WOCBP study participant and that the vasectomized partner has obtained partner of the WOCBP study participant and that the vasectomized partner has obtained medical assessment of surgical success for the procedure); and/or
    e. sexual abstinence† ‡

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25. Sexually active adult men who are unwilling to use the following forms of medically acceptable birth control: consistent use of a condom OR vasectomy with medical assessment of surgical success, for at least 90 days following study drug administration.

26. Is committed to an institution by virtue of an order issued either by the judicial or the administrative authorities.

27. Presents any concern to the study investigator that might confound the results of the study or poses an additional risk to the participant by their participation in the study.

28. Participated in any clinical research study evaluating another investigational drug including biologics or therapy, including specific immunotherapy, within 90 days or at least 5 halflives (whichever is longer) of an investigational biologic drug, or within at least 4 weeks for other investigational drug, prior to the screening visit.