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Pantoprazole in Patients at Risk for Gastrointestinal Bleeding in the ICU

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RobotReviewer report

trial	design	n	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment
Pantoprazolo in ICU.pdf	RCT	510	+	+	+	+

Characteristics of studies

Pantoprazolo in ICU.pdf

Population	1. Participants We screened patients 18 years of age or older who were admitted to the ICU for an acute condition (i.e., excluding elective admissions) and had at least one risk factor for clinically important gastrointestinal bleeding, including shock, use of anticoagulant agents, renal-replacement therapy, Pantopr azole in Patients at Risk for Bleeding mechanical ventilation (expected to last >24 hours), any history of liver disease, or any history of or ongoing coagulopathy (the full definitions of the criteria are provided in the Supplementary Appendix , available at NEJM.org 4,13). 2. METHODS In this European, multicenter, parallel-group, blinded trial, we randomly assigned adults who had been admitted to the ICU for an acute condition (i.e., an unplanned admission) and who were at risk for gastrointestinal bleeding to receive 40 mg of intravenous pantoprazole (a proton-pump inhibitor) or placebo daily during the ICU stay. 3. CONCLUSIONS Among adult patients in the ICU who were at risk for gastrointestinal bleeding, mortality at 90 days and the number of clinically important events were similar in those assigned to pantoprazole and those assigned to placebo.
Interventio n	1. A total of 3298 patients were enrolled; 1645 were randomly assigned to the pantoprazole group and 1653 to the placebo group. 2. METHODS In this European, multicenter, parallel-group, blinded trial, we randomly assigned adults who had been admitted to the ICU for an acute condition (i.e., an unplanned admission) and who were at risk for gastrointestinal bleeding to receive 40 mg of intravenous pantoprazole (a proton-pump inhibitor) or placebo daily during the

	ICU stay. 3. Interventions Enrolled patients received an intravenous injection of pantoprazole (40 mg suspended in 10 ml of 0.9% sodium chloride) or matching placebo (suspended in 10 ml of 0.9% sodium chloride) (Fig.
Outcomes	1. The primary outcome was death by 90 days after randomization. 2. The number of patients with infections or serious adverse reactions and the percentage of days alive without life support within 90 days were similar in the two groups. 3. The secondary outcomes were clinically important events in the ICU (defined as clinically important gastrointestinal bleeding, 4 new-onset pneumonia, 15 C. difficile infection, or acute myocardial ischemia; see the Supplementary Appendix); clinically important gastrointestinal bleeding in the ICU (defined as overt gastrointestinal bleeding and at least one of the following four features within 24 hours of gastrointestinal bleeding, in the absence of other causes, in the ICU: a spontaneous decrease in systolic blood pressure, mean arterial pressure, or diastolic blood pressure of 20 mm Hg or more; initiation of treatment with a vasopressor or a 20% increase in vasopressor dose; a decrease in hemoglobin of at least 2 g per deciliter [1.24 mmol per liter]; or transfusion of two or more units of packed red cells); infectious adverse events in the ICU (new-onset pneumonia or C. difficile infection); serious adverse reactions in the ICU (see the Supplementary Appendix); and the percentage of days alive without the use of life support (mechanical ventilation, circulatory support, or renal-replacement therapy; see the Supplementary Appendix) within the 90-day period.

Bias	Judgement	Support for judgement
Random sequence generation	low	1. Randomization was performed with a centralized, computer-generated allocation sequence stratified according to trial site and the presence or absence of active hematologic cancer. 2. Patients who were admitted to participating ICUs were screened and, if eligible, were randomly assigned in a 1:1 ratio, with the use of permuted blocks of varying sizes, to receive pantoprazole or placebo. 3. In most institutions, if the patient or legal guardian was unable to give consent initially, enrollment of patients was allowed on an emergency basis (e.g., with consent from a doctor who was independent of the trial), followed by consent from relatives and the patient to continue participation.
Allocation concealment	low	1. Randomization was performed with a centralized, computer-generated allocation sequence stratified according to trial site and the presence or absence of active hematologic cancer. 2. The trial-group assignments were concealed from the patients, clinicians, investigators, trial statisticians, and members of the data and safety monitoring committee. 3. The trial data were monitored at the sites by external monitors in accordance with the Good Clinical Practice directive of the European Union and centrally by staff from the coordinating center.
Blinding of participants and personnel	low	1. The trial-group assignments were concealed from the patients, clinicians, investigators, trial statisticians, and members of the data and safety monitoring committee. 2. Randomization was performed with a centralized, computer-generated allocation sequence stratified according to trial site and the presence or absence of active hematologic cancer. 3. From January 2016 through October 2017, a total of 3298 patients were enrolled in the trial; 1645 were randomly assigned to receive

		pantoprazole, and 1653 were assigned to receive placebo.
Blinding of outcome assessment	low	1. The trial-group assignments were concealed from the patients, clinicians, investigators, trial statisticians, and members of the data and safety monitoring committee. 2. Data for outcome measures were obtained from the patients' files by the trial investigators or their delegates. 3. The remaining 267 patients (130 in the pantoprazole group and 137 in the placebo group) who withdrew from the trial at their own or their surrogates' request allowed the use of their data, but 20 patients or surrogates in the pantoprazole group and 20 in the placebo group did not want further data to be registered except for data on mortality, which we obtained from registries.