

# Randomized Trial of a Clinical Dosing Algorithm to Start Anticoagulation with Phenprocoumon

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## Summary

**Question under study:** Prospective validation of two algorithms for the initiation of phenprocoumon treatment.

**Methods:** Inpatients with new-onset anticoagulation were randomized to one of two computer assisted dosing algorithms, or to a control arm. The primary outcome measure was the time to achieve therapeutic anticoagulation without overshooting (INR > 4.0 within 10 days). Secondary outcomes included overshooting INR values, death, or bleeding within 30 days. In addition, predictors of the dosing algorithms for the loading dose and the maintenance dose including genetic parameters were reassessed.

**Results:** 105 patients were randomized to arm A, 103 to arm B, and 93 to the control arm. Arms A and B needed a median of 7 days to reach a therapeutic INR, arm C 6 days (p=0.5). Overshooting INR was observed in 3.8%, 1.9% and 4.3% respectively (p=0.6). Bleeding was found in 0%, 1.9%, and 5.4% (p=0.06) and 30-day mortality was 0%, 1%, and 2.2% respectively (p=0.2). VKORC1:c.-1639G>A was associated with lower loading doses whereas VKORC1:c.-1453G>A needed higher doses. VKORC1:c.-1639G>A was also associated with lower maintenance doses.

**Conclusion:** Both algorithms allow safe initial dosing of phenprocoumon but they are not superior to anticoagulation by trained physicians. Dosing aids for coumarins with readily available clinical parameters may nevertheless be helpful for the use in polymorbid hospitalised patients. Clinical data and the INR-response to treatment provides powerful information and delaying initiation of anticoagulation while awaiting genetic tests is not expected to increase drug safety.

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**Key words:** randomized controlled trial; phenprocoumon; oral anticoagulation; coumarin; initiation of treatment; dosing; drug safety; hospital; pharmacogenetics; VKOR; loading dose, maintenance dos

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