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Edoxaban versus warfarin in atrial fibrillation patients with low, mid and high body weight: analysis of outcomes in the engage AF TIMI 48 trial

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On behalf: ENGAGE AF-TIMI 48

Topic(s):
Anticoagulants

Citation:
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Background: The impact on outcomes of oral anticoagulants in pts at extremes of body weight have not been well-characterized.

Aim: To analyse the outcomes of pts with atrial fibrillation (AF) enrolled in ENGAGE AF-TMI 48 randomized to warfarin (W) targeting INR 2.0–3.0, higher (HDE) or lower dose regimens of edoxaban (LDE), focusing on subgroups of patients at the extremes of weight.

Methods and results: Among 21105 pts enrolled in the trial we identified 3 subgroups: 1082 with low body weight (LBW) (<5th percentile, <55kg), 2153 with mid body weight (MBW) (45–55th percentile, 80–84 kg), and 1093 patients with high body weight (HBE) (>95th percentile, >120 kg). Baseline characteristics differed markedly (LWB pts were older and more likely Asian, women, with prior TIA/stroke, renal dysfunction) resulting in a trend towards higher rates of stroke/systemic embolism (SSE: 6.5% vs 4.7% in MBW vs 1.6% in HBW) and major bleeding (MB: 9.3% vs 7.7% in MBW vs 6.5% in HBW) in the warfarin arm. The risks of SSE (Pint = 0.52) were similar between W and HDE regardless of body weight, while the relative reduction in MB was greatest in LBW patients (HR reduction 45%, 23%, 1% across weight groups; Pint = 0.35) (Figure). Net clinical outcomes (SEE/major bleeding/death) tended to be most favourable for LBW pts (HR 0.67 [0.50–0.90]; Pint 0.084) (Figure).

Conclusions: In ENGAGE AF-TIMI 48 the profile of AF pts with LBW markedly differed suggesting a more fragile clinical status. Use of dose-adjusted edoxaban, as compared to W, was associated with similar efficacy regardless of weight, while bleeding and net outcomes were most favourable in LBW pts.
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Main outcomes during follow up

![Graphs showing outcomes for LBW, MBW, and HBW groups for primary efficacy end point: stroke/see, primary safety end point: major bleeding, and net clinical outcome: Stroke/SEE/Major Bleeding/Death.](image-url)