Profilassi del TEV nei pazienti oncologici ambulatoriali: la svolta degli studi AVERT e CASSINI

Background

- The role of thromboprophylaxis in the setting of outpatients treated with chemotherapy is still controversial.
- Recently the results of the AVERT and CASSINI trials, in which two direct oral anticoagulants (apixaban and rivaroxaban respectively) were tested for this indication, have been published.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Apixaban to Prevent Venous Thromboembolism in Patients with Cancer

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Methods

- Randomized, placebo-controlled, double-blind clinical trial assessing the efficacy and safety of apixaban (2.5 mg twice daily) for thromboprophylaxis in ambulatory patients with cancer who were at intermediate-to-high risk for venous thromboembolism (Khorana score, ≥2) and were initiating chemotherapy.
- The primary efficacy outcome was objectively documented venous thromboembolism over a follow-up period of 180 days.
- The main safety outcome was a major bleeding episode.

Results (I)

- 563 patients
- Venous thromboembolism occurred in 12 of 288 patients (4.2%) in the apixaban group and in 28 of 275 patients (10.2%) in the placebo group (P<0.001).
- In the modified intention-to-treat analysis, major bleeding occurred in 10 patients (3.5%) in the apixaban group and in 5 patients (1.8%) in the placebo group (hazard ratio, 2.00; 95% CI, 1.01 to 3.95; P = 0.046).
- During the treatment period, major bleeding occurred in 6 patients (2.1%) in the apixaban group and in 3 patients (1.1%) in the placebo group (hazard ratio, 1.89; 95% CI, 0.39 to 9.24).

Results (II)

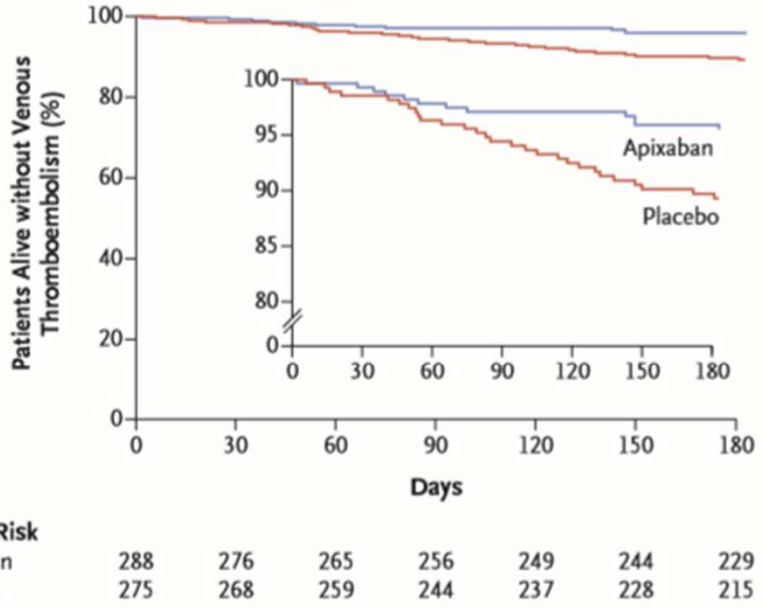

Figure 2. Kaplan–Meier Cumulative Event Rates of Venous Thromboembolism.
The inset shows the same data on an enlarged y axis.

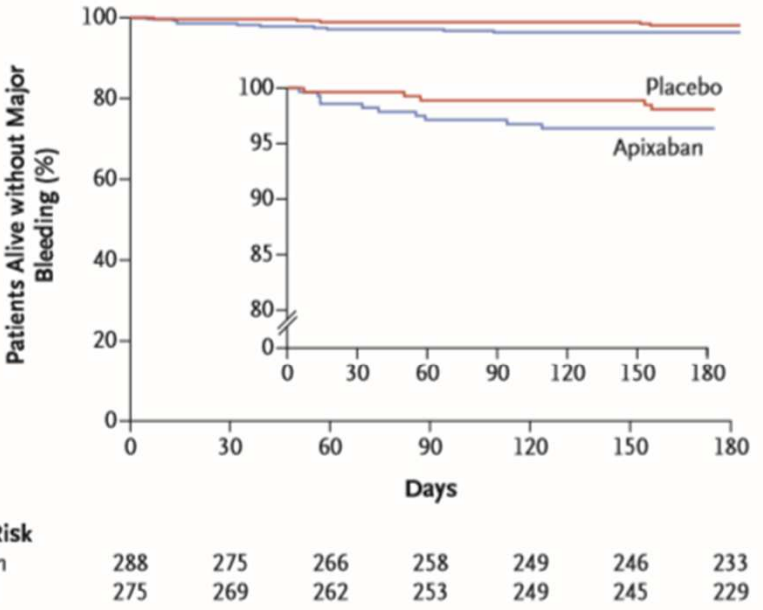

Figure 3. Kaplan–Meier Cumulative Event Rates of Major Bleeding.
The inset shows the same data on an enlarged y axis.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Rivaroxaban for Thromboprophylaxis in High-Risk Ambulatory Patients with Cancer

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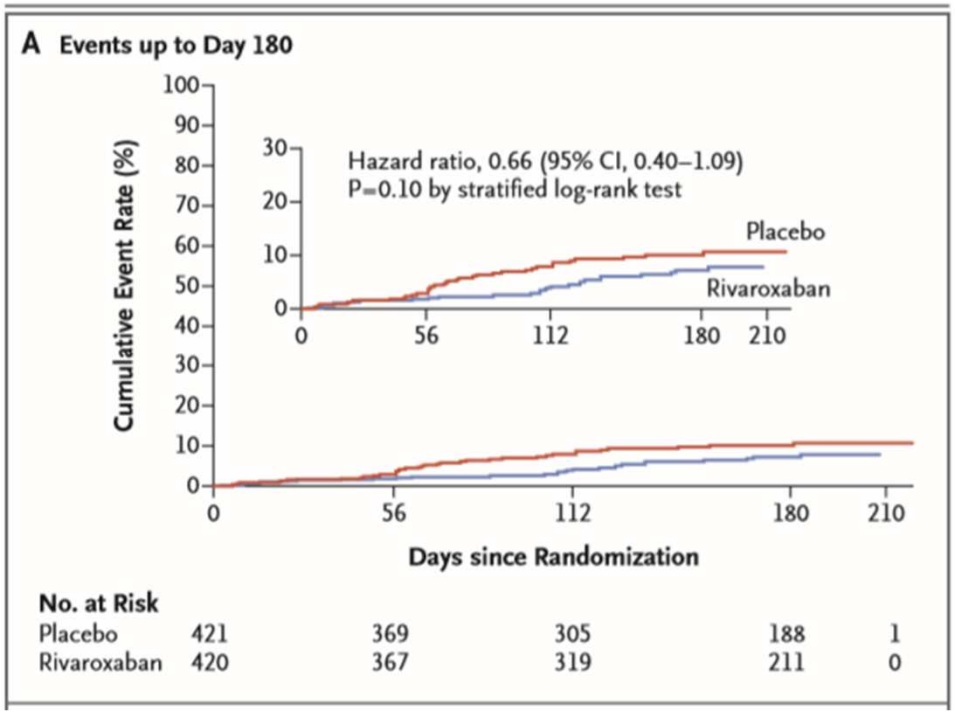
Methods

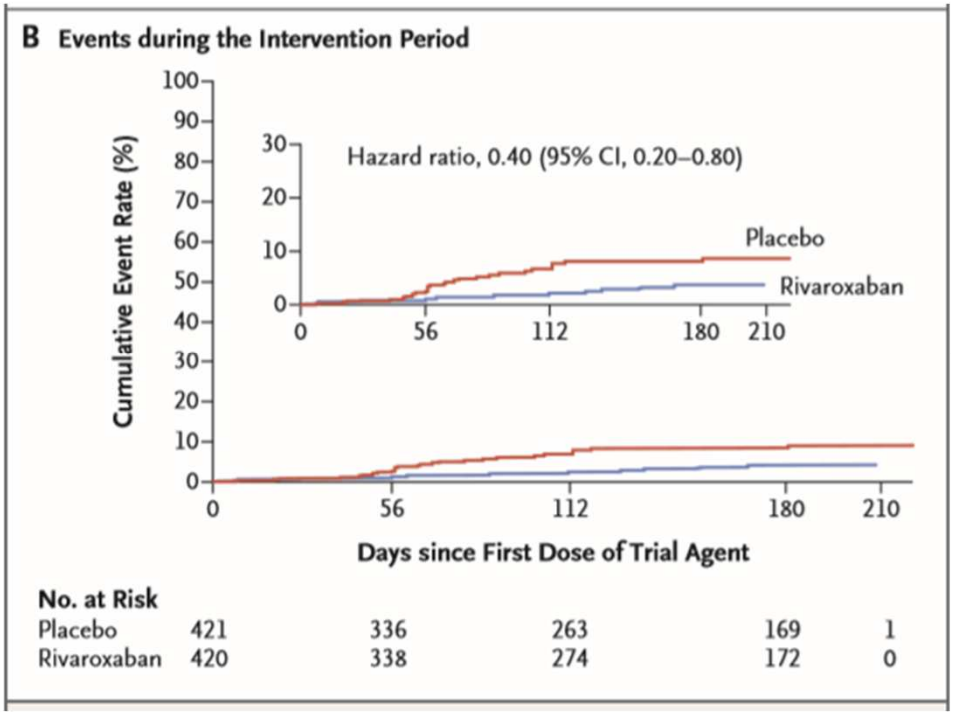
- Double-blind, randomized trial involving high-risk ambulatory patients with cancer (Khorana score of ≥2) assessing the efficacy and safety of rivaroxaban (at a dose of 10 mg/day) or placebo daily for thromboprophylaxis
- The primary efficacy end point was a composite of objectively confirmed proximal deep-vein thrombosis in a lower limb, pulmonary embolism, symptomatic deep vein thrombosis in an upper limb or distal deep-vein thrombosis in a lower limb, and death from venous thromboembolism for up to 180 days
- The primary safety end point was major bleeding

Results (I)

- 841 patients
- The primary end point occurred in 25 of 420 patients (6.0%) in the rivaroxaban group and in 37 of 421 (8.8%) in the placebo group (hazard ratio, 0.66; 95% confidence interval [CI], 0.40 to 1.09; P = 0.10) in the period up to day 180.
- In the prespecified intervention-period analysis, the primary end point occurred in 11 patients (2.6%) in the rivaroxaban group and in 27 (6.4%) in the placebo group (hazard ratio, 0.40; 95% CI, 0.20 to 0.80).
- Major bleeding occurred in 8 of 405 patients (2.0%) in the rivaroxaban group and in 4 of 404 (1.0%) in the placebo group (hazard ratio, 1.96; 95% CI, 0.59 to 6.49).

Results (II)


A Events up to Day 180
Cumulative Event Rate (%)
Hazard ratio, 0.66 (95% CI, 0.40–1.09)
P=0.10 by stratified log-rank test
Placebo
Rivaroxaban
Days since Randomization
No. at Risk
Placebo 421 369 305 188 1
Rivaroxaban 420 367 319 211 0


B Events during the Intervention Period
Cumulative Event Rate (%)
Hazard ratio, 0.40 (95% CI, 0.20–0.80)
Placebo
Rivaroxaban
Days since First Dose of Trial Agent
No. at Risk
Placebo 421 336 263 169 1
Rivaroxaban 420 338 274 172 0

Conclusions

- Both trials show that apixaban and rivaroxaban are effective and safe for the prophilaxis of venous thromboembolism in high risk ambulatory patients with cancer
- These data are destined to have a considerable scientific impact, as it could determine an epochal change in the approach to cancer patients