Direct Oral Anticoagulants for Treatment of Venous Thromboembolism in Patients with Hematological Malignancies

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Introduction

- **Cancer patients** are at **increased risk of venous thromboembolism** (VTE)[1] with higher recurrence and bleeding complications than in patients without cancer[2]
- Data is needed on **direct oral anticoagulants (DOACs)** for treatment of **VTE in hematological malignancies (HM).**
- Retrospective studies to date **lacked a control group** and included patients with atrial fibrillation and/or VTE, but not VTE alone.

Objective

To assess incidence of VTE recurrence and bleeding in HM patients treated with low molecular weight heparin (LMWH) or DOACs for acute VTE.

Methods

- **Retrospective cohort study** including patients with active HM and newly-diagnosed VTE treated at Rabin or Meir Medical Centers (1/2015-7/2021).
- Patients indexed on the first day of anticoagulation for VTE and followed for **12 months**.
- The **primary outcome** was a composite of:
  - Recurrent VTE
  - Clot progression
  - Major bleeding
  - Clinically relevant non-major bleeding (CRNMB).
- **Secondary outcomes:** individual components of the primary outcome
- **Analysis:** Cumulative incidence [95% confidence interval (CI)] calculated for each anticoagulation group (LMWH, DOAC). Hazard ratios (HR) calculated using cox-proportional hazards model. **Death** considered a **competing risk.**

Results

- 143 HM patients treated with **LMWH (96)** or **DOACs (47)** for acute VTE were included.
- HM was **lymphoma** in 83 (58%), **plasma cell dyscrasia** in 32 (22.3%)
- DOAC-treated patients were **older**, had **more pulmonary embolism** and less splanchnic vein thrombosis.

Table 1: **Patient characteristics**

Variable		DOACs**, n (%) [n=47]	LMWH n (%) [N=96]
Age at index (years) , median [IQR]		74 (66-81) *	69 (59-76)
Male sex		26 (55.3)	46 (47.9)
Hematological malignancy type	Lymphoma	26 (55.3)	57 (59.4)
	Plasma cell dyscrasia †	11 (23.4)	21 (21.8)
	Ph negative MPN ‡	8 (17)	13 (13.5)
	Chronic myeloid leukemia	1 (1)	1 (2.1)
	Acute leukemia	4 (4.2)	1 (2.1)
Newly diagnosed hematological malignancy (within 6 months)		19 (40.4)	46 (47.9)
Time since cancer diagnosis (days), median [IQR]		273 (0-2102)	161 (13.5-2078.5)
Allogeneic hematopoietic stem cell transplantation §		1 (2.1)	5 (5.2)
VTE site §	Pulmonary embolism	23 (48.9) *	32 (33.3)
	Lower extremity DVT	20 (42.5)	43 (44.8)
	Upper extremity DVT	7 (14.9)	19 (19.8)
	Splanchnic vein thrombosis	0 *	11 (11.5)
	Other	0	3 (3.1)
VTE-BLEED score, median [IQR]		5 (3.5-6)	5 (3.5-5.5)
Renal insufficiency (eGFR<60 ml/min)		13 (27.7)	16 (16.7)
Concomitant antiplatelet treatment		9 (19.1)	13 (13.5)
Platelet count ($X10^9$) at index, median [IQR]		225 (135-317)	207 (128-310)

* P value < 0.05 for comparison with LMWH group
† All patients had multiple myeloma, except 1 patient with smoldering myeloma
‡ Including polycythemia vera, essential thrombocytosis, myelofibrosis and MPN unclassifiable
§ Some patients had multiple VTE sites
** DOAC type: Apixaban 27/47 (57.4%), Rivaroxaban 20/47 (42.5%)
DOAC, direct oral anticoagulants; *DVT*, deep vein thrombosis; *eGFR*, estimated glomerular filtration rate; *IQR*, interquartile range; *LMWH*, low molecular weight heparin; *MPN*, myeloproliferative neoplasm; *VTE*, venous thromboembolism

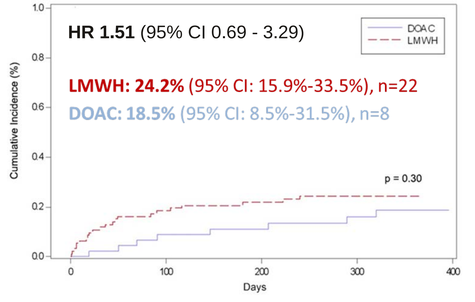


Figure 1: 12-month cumulative incidence of **recurrent VTE, clot progression, major bleeding or CRNMB**

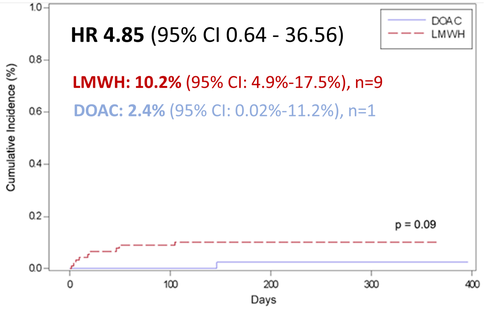


Figure 2: 12-month cumulative incidence of **major bleeding**

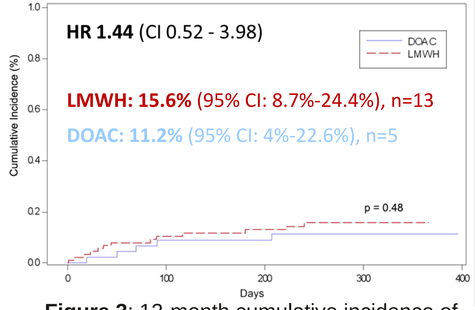


Figure 3: 12-month cumulative incidence of **CRNMB**

Conclusions

- This study **generates the hypothesis that DOACs may be a safe and effective alternative** to LMWH for VTE in patients with lymphoma or plasma cell dyscrasia.
- Larger prospective studies needed to confirm these findings.

References

1. Lee AYY, Levine MN. *Circulation* 2003;107.
2. Prandoni P et al. *Blood* 2002;100(10):3484–8.
3. Bleker SM et al.*Thromb Haemost* 2017;117(10):1944–51