



TERAPIE ANTICOAGULANTI E GESTIONE DELLE
COMPLICANZE

EXTENDED ANTICOAGULATION WITH DOACS IN PATIENTS AFFECTED BY HEMATOLOGIC MALIGNANCIES AND VENOUS THROMBOEMBOLISM: DOES LOW DOSE FIT ALL?

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Background and Aims. Data on the extended treatment of venous thromboembolism (VTE) in the oncohematologic patients is lacking. The aim of our monocentric retrospective analysis was to evaluate the efficacy and safety in secondary prophylaxis of two different Direct Oral Anticoagulants (DOACs) treatment strategies (full-dose/low-dose) in onco-hematologic patients, based on the persistence of complete venous occlusion.

Methods. We included adult oncohematologic patients with objectively confirmed VTE and at least 12 months of follow-up from the start of DOAC treatment. During the acute-phase of VTE treatment (first 3-6 months), the patients were treated with therapeutic dose of anticoagulants. In the extended therapy, the patients were treated with full-dose DOAC in case of persistent complete thrombosis and with low-dose DOAC in case of partial or complete vein recanalization and active cancer. Follow-up visits were scheduled every three months and included monitoring for bleeding (B-AEs) and thrombotic adverse events (T-AEs). Imaging with doppler ultrasound or computed tomography was performed every six months as per institutional policy, or earlier if recurrence was suspected. B-AEs were classified according to the ISTH criteria.

Results. Patients' characteristics and AEs are summarized in Table 1. Fourteen bleeding events (87.5%) occurred during full-dose treatment (1 major [severe metrorrhagia] and 13 CRNM) and 2 (12.5%) during low-dose treatment (1 major [cerebral hemorrhage], 1 CRNM). The 13 CRNM events during full-dose included 10 gastrointestinal bleedings, 1 epistaxis, 1 mild metrorrhagia and 1 hematuria associated with bladder catheter placement. The CRNM event during low-dose was a conjunctival bleeding. During extended phase, the incidence rates of B-AEs were 9.9 per 100 patient-years for full-dose therapy and 0.8 per 100 patient-years for low-dose therapy. Nine patients (6.1%) experienced recurrent thrombosis during extended therapy with DOACs, including 6 (66.7%) on full-dose and 3 (33.3%) on low-dose. During extended phase, the incidence rates of T-AEs were 4.3 versus 1.3 per 100 patient-years, respectively. During

follow-up, five patients experienced a platelet count reduction between $50 \times 10^9/L$ and $100 \times 10^9/L$, while none had counts below $50 \times 10^9/L$.

Conclusions. Despite the indication bias inherent in this retrospective design, our findings suggest that in onco-hematologic patients, full-dose therapy may be appropriate for those with persistent complete venous occlusion due to a higher baseline risk of recurrence, which appears to remain significant over time: the higher incidence rate of T-AEs during full dose DOAC in the extended treatment could be accounted to a higher thrombotic risk associated with no vein recanalization. De-escalation to reduced-dose DOACs after vein recanalization appeared to reduce the incidence of bleeding events, particularly CRNM B-AEs.

Patients' characteristics	N (%) ^a
Sex	
Male	78 (52.7)
Female	70 (47.3)
Age (years at thrombosis) - Median (range)	65.3 (18.9-90.9)
Type of VTE	
Typical site	96 (64.9)
Atypical site	47 (31.7)
PECC-related	5 (3.4)
Onco-hematologic disease	
MPN	61 (41.2)
Lymphoma	55 (37.2)
MM	17 (11.3)
PNH ± Aplastic anemia	8 (5.4)
AL	4 (2.7)
MDS	3 (2)
Acute treatment of VTE	
DOACs	119 (80.5)
Apixaban	59 (39.9)
Edoxaban	38 (25.7)
Rivaroxaban	22 (14.9)
VKA	29 (19.5)
DOACs dosage during extended treatment of VTE	
Full dose DOACs	29 (19.5)
Full dose DOACs → low dose DOACs ^b	97 (65.4)
Low dose DOACs	22 (15.1)
Duration of extended treatment of VTE (months) - Median (range)	35.3 (12.8-119.4)
Duration of full dose DOACs (months) during extended treatment of VTE ^c - Median (range)	13.4 (0.1-125.4)
Time from full dose to low dose DOACs (months) during extended treatment of VTE ^c - Median (range)	12.2 (0.5-100.1)
Duration of low dose DOACs (months) during extended treatment of VTE ^c - Median (range)	24.2 (1.3-109.4)
Bleeding adverse events (full dose DOACs vs low dose DOACs) - Rate per 100 patient-years	
Major	0.7 vs 0.4
CRNM	9.2 vs 0.4
Thrombotic adverse events - Rate per 100 patient-years	
During full dose DOACs	4.3
During low dose DOACs	1.3

VTE, venous thromboembolism; PECC, peripherally inserted central catheter; MPN, myeloproliferative neoplasm; MM, multiple myeloma; PNH, paroxysmal nocturnal hemoglobinuria; AL, acute leukemia; MDS, myelodysplastic neoplasm; LADVT, low molecular weight heparin; DOACs, direct oral anticoagulants; VKA, vitamin K antagonists; CRNM, clinically relevant non-major bleeding.

^aIf not otherwise specified.

^bPatients were switched to low dose after partial or complete vein recanalization and persistence of active cancer.

^cIf applicable.