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Oral Anticoagulants for the Treatment of Venous Thromboembolism in patients with cancer

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Background/Aims: Venous thromboembolism (VTE) is one of the highly prevalent complications in cancer patients. Based on the current guideline, treatment options for cancer-associated thrombosis include low molecular weight heparin (LMWH), unfractionated heparin (UFH), warfarin, and fondaparinux. However, VKA has severe disadvantages due to the need of regular blood level monitoring, limited therapeutic range, and variable drug-drug interactions and the use of LMWH is meanwhile limited by the requirement of daily subcutaneous injection. Recently, direct-acting oral anticoagulants (DOAC) have emerged as attractive alternatives for VTE. In this study, we aimed to compare efficacy and safety between DOAC and VKA and LMWH using a network meta-analysis (DOAC vs. VKA vs. LMWH). **Methods:** We conducted a systematic literature review to identify all eligible randomized controlled trials (RCT) by searching PubMed, Web of Science, ASH, ASCO, EHA, and ESMO databases. The network meta-analysis was performed using a multivariate random effect model under a frequentist framework. We evaluated which treatment is most effective on reducing a risk of recurrent VTE and major bleeding by NMA. **Results:** Four DOACs were identified in six RCTs. When comparing the efficacy between VKA and DOACs, the recurrence rate of VTE was lower in the treatment with DOACs than with VKA, but not statistically significant (Figure 1A). In safety, the risk of major bleeding was relatively low in the use of DOACs compared to VKA, except for edoxaban (edoxaban: OR 1.63, 95% CrI 0.55-4.85) (Figure 1B). The SUCRA curves for each drug by ranking probability were displayed in Figure 2. The treatment with the highest SUCRA value was Rivaroxaban. In case of major bleeding, the treatment with the highest SUCRA value was Apixaban. **Conclusions:** For the treatment of VTE in cancer patients, DOAC has a favorable tendency for the efficacy and safety compared to VKA. DOACs could be one of the standard treatment options for management of VTE in cancer patients. Among DOACs, apixaban has a relatively good outcome.

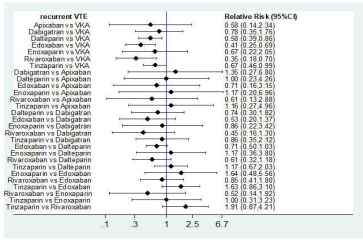

Figure 1A. Forest plot for VTE

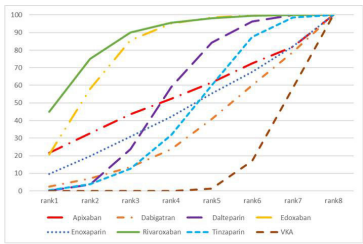

Figure 2A. SUCRA curve for VTE

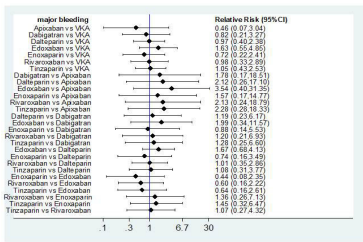

Figure 1B. Forest plot for major bleeding

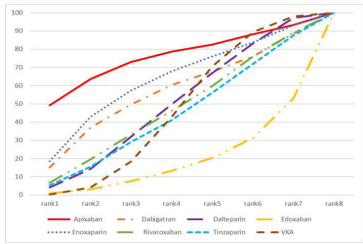

Figure 2B. SUCRA curve for Bleeding

■ Sat-362 ■

Clinical experiences of daratumumab monotherapy for relapsed or refractory multiple myeloma in Korea

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Background/Aims: Despite well-known efficacy of daratumumab monotherapy for relapsed or refractory multiple myeloma through phase 1 and 2 clinical trials (GEN501 and SIRIUS), outcomes in real practice following daratumumab monotherapy have yet to be investigated. **Methods:** A multicenter retrospective study of 16 Korean patients receiving daratumumab monotherapy for relapsed or refractory multiple myeloma was conducted. All patients received ≥2 prior lines of therapy for multiple myeloma. **Results:** With a median seven treatment cycles given to patients, an overall response was shown in nine of 16 patients (overall response rate, 56.3%, table 1). Three patients with creatinine clearance 〈30ml/min even achieved an overall response. The median progression-free survival (PFS) was 2.7 months with 28.9% (95% CI, 9.0-52.8) of six-month PFS. All infusion-related reactions, including ≥grade 3 back pain (6.3%) and dyspnea (6.3%), were manageable. The most common hematologic and non-hematological adverse events were anemia (62.5%) and upper respiratory infection (43.8%). ≥grade 3 bacterial infectious adverse events were identified, including upper and lower respiratory infection (12.5% and 18.8%) and death following sepsis (6.3%) (Table 2). **Conclusions:** We observed favorable outcomes of daratumumab monotherapy in Korean patients with relapsed or refractory multiple myeloma. Nevertheless, prophylactic antibiotics could be considered as well when administering daratumumab monotherapy.

Table 1. Overall best response

	No. (%)
Overall response	9 (56.3%)
Complete response	4 (25.0%)
Very good partial response	0 (0.0%)
Partial response	5 (31.3%)
Minimal response	2 (12.5%)
Stable disease	3 (18.8%)
Refractory	1 (6.3%)
Unknown*	1 (6.3%)

*: Response cannot be assessed due to early death by sepsis during first cycle of daratumumab monotherapy

Table 2. Infusion-related reactions and adverse events

	Any grade	Grade 3 or higher
Infusion-related reactions		
Fatigue	4 (25.0%)	0 (0.0%)
Fever	2 (12.5%)	0 (0.0%)
Cough	3 (18.8%)	0 (0.0%)
Chill	3 (18.8%)	0 (0.0%)
Allergic rhinitis	1 (6.3%)	0 (0.0%)
Back pain	1 (6.3%)	1 (6.3%)
Dyspnea	3 (18.8%)	1 (6.3%)
Hematological adverse events		
Anemia	10 (62.5%)	6 (37.5%)
Neutropenia	4 (25.0%)	4 (25.0%)
Thrombocytopenia	2 (12.5%)	1 (6.3%)
Non-hematological adverse events		
Upper respiratory infection	7 (43.8%)	2 (12.5%)
Lower respiratory infection	3 (18.8%)	3 (18.8%)
Bacteremia	1 (6.3%)	1 (6.3%)
Diarrhea	1 (6.3%)	0 (0.0%)
Elevation of liver enzyme	1 (6.3%)	0 (0.0%)