



# Interaction table of oral factor Xa inhibitors with oral anti-cancer drugs

GSASA Congress 2022  
Lucerne, 09.11.2022  
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# **Conflict of interest**

- Minority ownership in one public pharmacy in Slovakia
- Membership in GSASA, Slovak Chamber of Pharmacists

# Agenda

1. Anticoagulation in cancer patients, cancer-associated thrombosis (CAT)
2. Oral factor Xa inhibitors and their metabolic pathways
3. Interaction table – methodology
4. Interaction table and its practical aspects/take-home message

# Anticoagulation in cancer patients, CAT

## Epidemiology

	cancer patients	cancer patients + chemo
VTE incidence*	4 fold higher	6.5 fold higher
VTE recurrence*	4-7 fold higher	

\*compared to **general** population

+/- concomitant disease, e.g. atrial fibrillation



Anticoagulation indicated

Zahir et al (2017): Incidence of Venous Thromboembolism in cancer patients treated with Cisplatin based chemotherapy — a cohort study. <https://doi.org/10.1186/s12885-016-3032-4>  
Heit et al (2000): Risk Factors for Deep Vein Thrombosis and Pulmonary Embolism. A Population-Based Case-Control Study. doi:10.1001/archinte.160.6.809

# Anticoagulation in cancer patients, CAT

## Trials with direct oral anticoagulants (DOAC) in CAT

	trial	comparator	results	bleeding risk
<b>apixaban</b>	Caravaggio	dalteparin	noninferior	~
<b>edoxaban</b>	Hokusai VTE Cancer	dalteparin	noninferior	↑
<b>rivaroxaban</b>	SELECT-D	dalteparin	reduced rate of recurrent VTE compared with LMWH	↑
	CASSINI	placebo ( <b>primary</b> prev.)	substantially lower incidence	↑
<b>dabigatran</b>	<b>currently no</b> double-blind RCT performed to assess efficacy and safety in cancer patients			

Agnelli G et al (2020): Apixaban for the Treatment of Venous Thromboembolism Associated with Cancer. DOI: 10.1056/NEJMoa1915103

Young AM et al (2018): Comparison of an Oral Factor Xa Inhibitor With Low Molecular Weight Heparin in Patients With Cancer With Venous Thromboembolism: Results of a Randomized Trial (SELECT-D). DOI: 10.1200/JCO.2018.78.8034

Khorana AA et al (2019): Rivaroxaban for Thromboprophylaxis in High-Risk Ambulatory Patients with Cancer. DOI: 10.1056/NEJMoa1814630

Raskob GE et al (2018): Edoxaban for the Treatment of Cancer-Associated Venous Thromboembolism. DOI: 10.1056/NEJMoa1711948

# Oral factor Xa inhibitors and their metabolic pathways

## Possibility of DDIs

	CYP3A4	P-gp	BRCA
<b>apixaban</b>	main	substrate	substrate
<b>edoxaban</b>	negligible	substrate	-
<b>rivaroxaban</b>	main	substrate	substrate

EMA: SmPCs Eliquis/Lixiana/Xarelto, [www.ema.europa.eu](http://www.ema.europa.eu)

# Interaction table – methodology

- 67 oral anti-cancer drugs screened: EMA/Swissmedic/FDA/UpToDate/DrugBank
  - PubMed search
- ↓
- management of DDIs

Clinically relevant interaction not expected or manageable by dose reduction
Oral anti-cancer drug is a substrate of CYP3A4: interaction with Edoxaban not expected
Concomitant use not recommended (not necessarily a contraindication); if injection refused by patient, contact Clinical Pharmacy service

- no intervention/dose reduction of apixaban
- preferred choice
- switching to other drug within therapeutic class
- avoiding the combination (LMWH is the 1<sup>st</sup> choice)

- ✓ double-check by another clinical pharmacist
- ✓ reviewed by chief clinical pharmacist and chief haemato-oncologist

# Interaction table – methodology

	Clinically relevant interaction not expected or manageable by dose reduction (if applicable)
preferred	Oral anti-cancer drug is a substrate of CYP3A4: interaction with Edoxaban not expected and it is a preferred choice
	Concomitant use not recommended (not necessarily a contraindication); LMWH is the 1st choice) - if injection refused by patient, contact Clinical Pharmacy service
	Bleeding risk by the anti-cancer drug itself; detailed description, if applicable



Oral anti-cancer drug	Oral factor Xa inhibitors			Increased bleeding risk by the oral anti-cancer drug itself?
	Apixaban	Edoxaban	Rivaroxaban	
Abiraterone		preferred		
Afatinib				
Alectinib		preferred		
Anagrelide				
Anastrozole		preferred		vaginal bleeding
Axitinib		preferred		
Bicalutamide		preferred		
Bosutinib		preferred		
Brigatinib				
Cabozantinib	Dose reduction 25%	preferred		

# **Interaction table – practical aspects**

- easy-to-use (traffic-light system)
- already on the internet page of our hospital pharmacy available
- future implementation into clinic information system/web-based tool?

# Take-home message

## Goals

- efficiency ↑
- patient safety ↑
- quality of healthcare ↑



Standardized management of the DDIs  
within our hospital

## Interdisciplinary approach

- acceptance ↑
- feedback from physicians (of high value)

- regular update crucial (new evidence!)



# Vielen Dank für Ihre Aufmerksamkeit!

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