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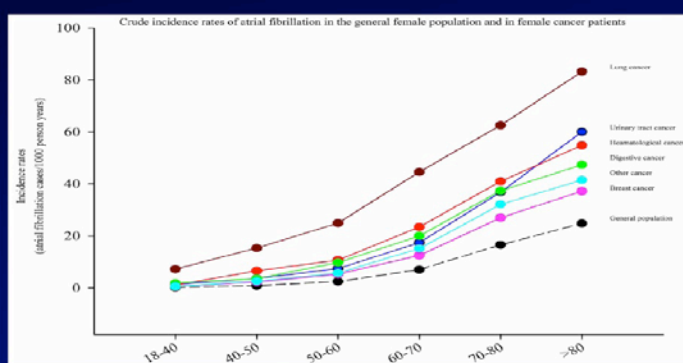
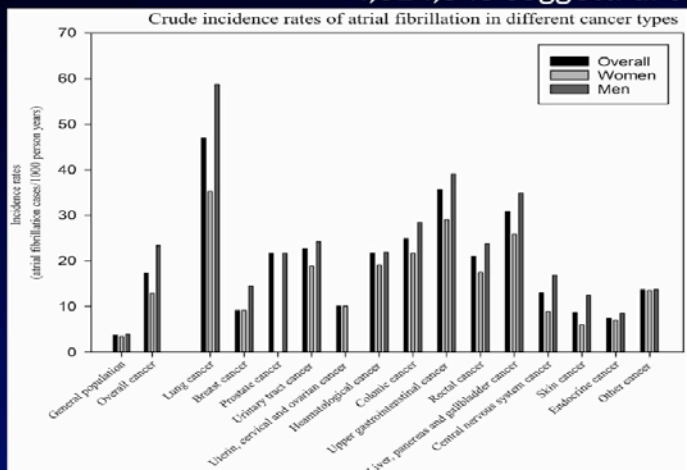


SAPIENZA
UNIVERSITÀ DI ROMA



Incidenza di FA in pazienti con neoplasie

4,324,545 soggetti di cui 316,040 con neoplasie



Jakobsen et al. BMC Cancer (2019) 19:1105

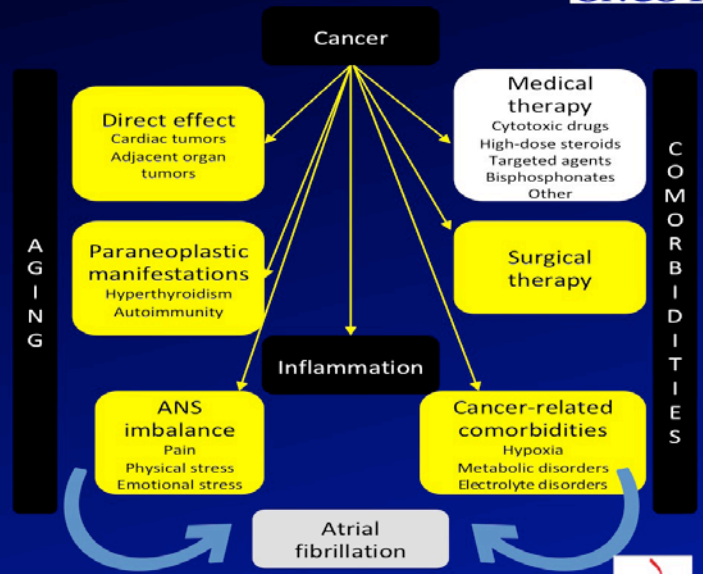


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- Inflammatory response in neoplastic processes
- Hyperadrenergic state
- Metabolic and electrolyte derangements
- Metastatic involvement of cardiac structures
- Paraneoplastic syndromes
- Chemotherapeutic agents



Farmakis D, et al. J Am Coll Cardiol. 2014;63:945-53
ANS, autonomous nervous system



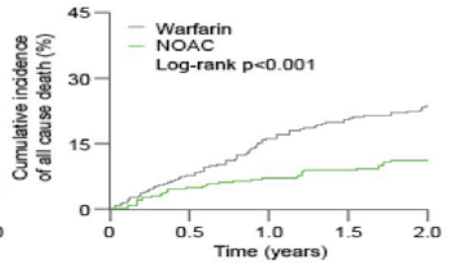
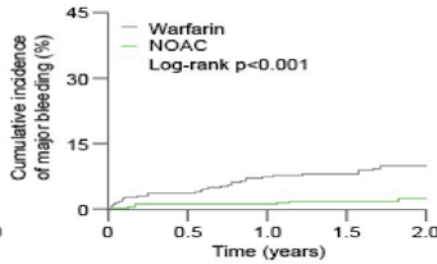
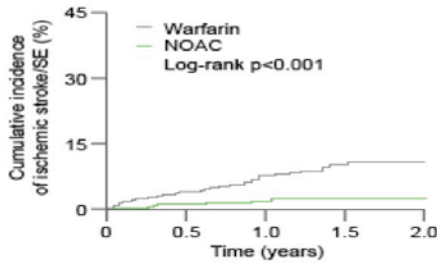
Complicanze tromboemboliche e di sanguinamento in pazienti con neoplasie e FA

N° eventi (%/anno)	ROCKET (2010)		ARISTOTLE (2010)		ENGAGE (2016)	
	SI	NO	SI	NO	SI	NO
ICTUS ISCHEMICO	12 (2.03)	196 (1.62)	9 (0.8)	166 (1.1)	21 (2.08)	214 (2.08)
SANGUINAMENTO MAGGIORE E NMCR	96 (21.59)	1353 (14.19)	67 (6.9)	810 (5.9)	174 (27.94)	1636 (12.49)
SANGUINAMENTO MAGGIORE	33 (6.44)	353 (3.31)	32 (3.2)	430 (3.1)	63 (8.18)	494 (3.34)
TUTTI I SANGUINAMENTI (MAGGIORI, NMCR, MINORI)	152 (40.79)	2132 (24.97)	245 (32.2)	2815 (25.4)	195 (33.82)	1969 (15.77)



Real life

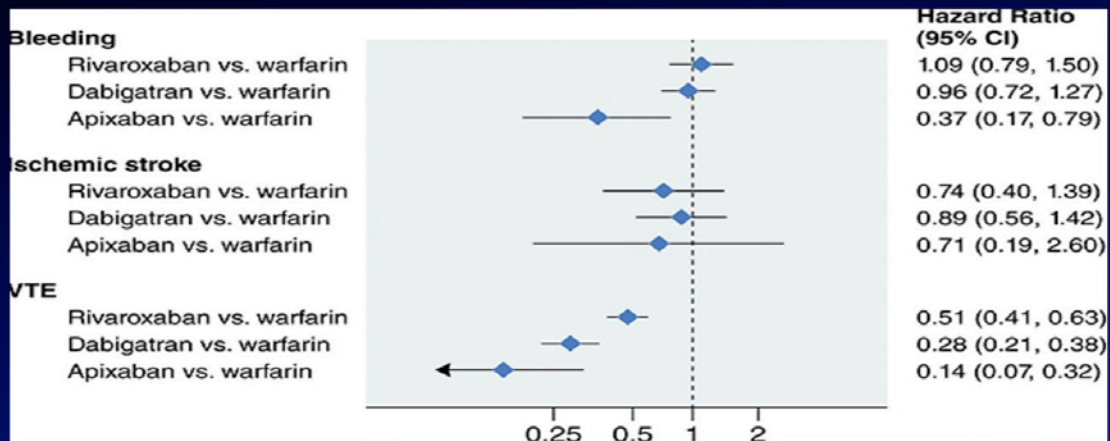
- In 2,568 consecutive AF patients with newly diagnosed cancer, stroke/systemic embolism (SE), major bleeding, and all-cause death were analysed.
- NOACs have significantly lower incidences of ischemic stroke/systemic embolism ($p < 0.001$), major bleeding ($p < 0.001$), and all-cause death ($p < 0.001$) than warfarin
 - The incidence of major bleeding was particularly lower within 1 year after cancer diagnosis
 - The incidences of all clinical events were significantly lower in the NOAC group vs warfarin group



Kim et al. Korean Circ J. 2018;48:406-17.

DOACs in cancer and AF

MarketScan databases, we identified 16 096 AF patients (mean age, 74 years) initiating oral anticoagulant and being actively treated for cancer





Drug-Drug Interactions of NOACs in Cancer Patients



Table 15. Anticipated effects of common anticancer drugs on non-vitamin K antagonist oral anticoagulants plasma levels

Drug Class	Warfarin	Dabigatran esters	Apixaban	Edoxaban	Rivaroxaban
P-gp substrate		Yes			
CYP3A4 substrate		No			
Antibiotic agents					
Penicillin	Moderate CYP3A4 inhibition, CYP3A4P-gp competition				
Vancomycin	Strong P-gp induction, CYP3A4P-gp competition				
Doxorubicin, Vincristine	Mild CYP3A4 induction, CYP3A4P-gp competition				
Vincoreline	Mild CYP3A4 induction, CYP3A4P-gp competition				
Antimetabolites					
Metoprolol	P-gp competition, no relevant interaction anticipated				
Fluorouracil, Purine analogs, Pyrimidine analogs	No relevant interaction anticipated				
Topoisomerase inhibitors					
Topotecan	No relevant interaction anticipated				
Vincristin	CYP3A4P-gp competition, No relevant interaction anticipated				
Etoposide	Mild CYP3A4 inhibition, CYP3A4P-gp competition				
Androgen/antiandrogen					
Desvenlafaxine	Strong P-gp induction, mild CYP3A4 inhibition, CYP3A4P-gp competition				
Mandipin	Mild CYP3A4 inhibition, P-gp competition				
Dienverdin					
Misoxantrone					
Ablating agents					
Irinotecan	Mild CYP3A4 inhibition				
Capecitabine	Mild CYP3A4 inhibition				
Letrozole	Mild CYP3A4 inhibition				
Bosutinib	No relevant interaction				
Bevacizumab	No relevant interaction				
Chemotherapy	No relevant interaction				
Platinum-based agents					
Cisplatin, Carboplatin, Oxaliplatin	No relevant interaction				
Immunomodulating agents					
Bendamustine	P-gp competition, no relevant interaction anticipated				
Chlorambucil, Melphalan, Carmustine, Procarbazine, Dacarbazine, Teniposide	No relevant interaction				
Hormonal agents					
Abiraterone	Moderate CYP3A4 inhibition, strong P-gp inhibition, CYP3A4P-gp competition				
Enzalutamide	Strong CYP3A4 inhibition, strong P-gp inhibition, CYP3A4P-gp competition				
Bicalutamide	Moderate CYP3A4 inhibition				
Tamoxifen	Strong P-gp inhibition, mild CYP3A4 inhibition, CYP3A4P-gp competition				
Androstanoles	Mild CYP3A4 inhibition				
Flutamide	CYP3A4 competition, No relevant interaction anticipated				
Leuprorelin, Mitotane	No relevant interaction anticipated				
Enzyme-modulating agents					
Etoposidine	Strong to moderate P-gp inhibition, moderate CYP3A4 inhibition, CYP3A4P-gp competition				
Docetaxel	Strong CYP3A4P-gp induction, CYP3A4P-gp competition				
Taxotene	Strong to moderate P-gp induction, mild CYP3A4 inhibition, CYP3A4P-gp competition				
Prezista	Moderate CYP3A4 induction, CYP3A4P-gp competition				
Tamoxifen, Endoxan	Mild CYP3A4 inhibition, CYP3A4P-gp competition				
Endoxan	CYP3A4 competition, No relevant interaction anticipated				

2018 ESC AF GUIDELINES



Obiettivi

- **Ricerca evidenze cliniche sulle interazioni farmacologiche**
- **Valutare efficacia e sicurezza dei diversi trattamenti anticoagulanti**
- **Migliorare le conoscenze nella gestione del paziente affetto da FA e cancro**



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