

Table 3: Drug-Drug Interactions of Common Chemotherapeutic Agents and Antithrombotic Agents*†

	Mechanism	Edoxaban	Rivaroxaban	Clopidogrel	Ticagrelor	Prasugrel
P-gp		S	S		S, I	
CYP3A4			S		S, I (weak)	
Common Chemotherapeutic Agents						
<i>Lapatinib</i> <i>Neratinib</i> <i>Sunitinib</i> <i>Vandetanib</i> <i>Vemurafenib</i>	P-gp inhibition	↑ edoxaban exposure; consider alternative anticoagulant	↑ rivaroxaban exposure. No action needed because not clinically significant unless significant renal impairment. Avoid combination with strong CYP3A4 inhibitor.			
<i>Crizotinib</i> <i>Imatinib</i> <i>Nilotinib</i> <i>Ribociclib</i>	CYP3A4 inhibition (moderate)		↑ rivaroxaban exposure. No action needed because not clinically significant unless significant renal impairment. Avoid combination with P-gp inhibitor.		↑ ticagrelor exposure. Monitor for increased adverse effects (i.e., bleeding). No dose adjustment recommended.	
<i>Doxorubicin</i>	P-gp and CYP3A4 inhibition				↑ doxorubicin exposure. Consider alternative antiplatelet agent during chemotherapy. If concomitant therapy is necessary, monitor for toxicities.	
<i>Dabrafenib</i> <i>Ivosidenib</i>	CYP3A4 induction		↓ rivaroxaban concentration. Consider alternative anticoagulant during chemotherapy.		↓ ticagrelor concentration. Consider alternative antiplatelet agent during chemotherapy.	
<i>Enzalutamide</i>			↓ rivaroxaban concentration (significant). Avoid concomitant use; use		↓ ticagrelor concentration (significant). Avoid concomitant use;	

			alternative anticoagulant.		use alternative antiplatelet agent.	
Paclitaxel	CYP2C8 inhibition			↑ paclitaxel exposure. If concomitant therapy is necessary, monitor for toxicities (i.e., severe neuropathy, neutropenia).		
Dasatinib Ibrutinib Ibritumomab Nintedanib Obinutuzumab	Additive clinical effect	↑ antithrombotic effects and increased risk of bleeding. Consider the benefit to risk ratio of antithrombotic therapy. If concomitant therapy is necessary, use caution and frequently monitor platelet counts and evidence of bleeding or hemorrhagic events.				

* Drug in *italics* represents enzyme inhibitor in proposed interaction.

† Color denotes severity of interaction as follows:

- *Red*. Major interaction; Black Box warning and/or strong clinical effects; avoid combination.
- *Orange*. Moderate interaction; known, reliable mechanism of interaction such as enzyme effects, protein binding, etc. Data demonstrate that there is a clinically significant drug interaction. Individual risk-benefit assessment for each patient should be considered with concomitant therapy. Actions such as aggressive monitoring or empiric dose changes should be taken to minimize toxicity. Alternative agents should be chosen if risks outweigh benefits.
- *Yellow*. Minor interaction; potential interaction between the agents; however, benefits usually outweigh risks. Evidence may be limited to only case reports. Appropriate monitoring plan should be implemented; a small number of patients may need dose adjustments or consideration of alternative agent.