Table 1: Drug-Drug Interactions of Common Cardiac Drugs and Chemotherapeutic Agents*

Cardiac Drug(s)	Enzyme/ Action	Chemotherapy Drug†	Effect of Drug- Drug Interaction	Suggested Oncologist Management	Suggested Cardiologist Management	
Beta-Blockers						
All beta- blockers	Additive clinical effect	Crizotinib	Additive bradycardia	Avoid using the combination of ceritinib with beta- blockers. If concomitant use is necessary and symptomati bradycardia occurs, hold ceritinib, adjust or discontinue the beta-blocker, and upon recovery resume ceritinib at a reduced dose with frequent monitoring of heart rate.‡ Monitor blood pressure and heart rate regularly. Dose reduction or discontinuation of one of the agents may be necessary if clinically significant bradycardia occurs.‡		
Carvedilol	P-gp inhibition (moderate)	Afatinib	↑ chemotherapy drug concentration	Monitor for adverse effects of afatinib. If not well-tolerated, decrease afatinib daily dose by 10 mg. Monitor for adverse	Consider alternative agent if possible. Consider alternative agent if	
		Nilotinib Paclitaxel Pazopanib Vincristine Vinblastine		effects of chemotherapy drug if concomitant therapy is necessary.	possible. If carvedilol is used for prevention of anthracycline cardiotoxicity, individual risk vs. benefit must be considered. If concomitant therapy is necessary and drug-drug interaction involves QT-prolonging chemotherapy drug, ensure appropriate electrocardiographic (ECG) and electrolyte monitoring.	
Carvedilol; metoprolol	CYP2D6 inhibition (moderate)	Imatinib Panobinostat	个 beta-blocker concentration	Monitor blood pressure and heart rate. Notify cardiologist if clinically significant bradycardia or hypotension occurs	Monitor blood pressure and heart rate closely if concomitant therapy is necessary. Dose reduction or discontinuation of carvedilol may be necessary if clinically significant bradycardia or hypotension occurs	
ACEi/ARBss						
Losartan; Irbesartan	CYP2C9 inhibition (moderate)	Ceritinib	个 losartan or irbesartan concentration		Monitor for evidence of increased adverse effects or toxicity due to ARB. Dose reduction or alternative agent may be necessary.	
Losartan	CYP3A4 inhibition (strong)	Idelalisib	个 losartan concentration	Notify cardiologist/ prescriber to switch to alternative therapy.	Avoid co-administration. Consider alternative agent during idelalisib therapy that does not undergo CYP3A4 metabolism (i.e., irbesartan, valsartan)	

Losartan	CYP2C9 induction	Dabrafenib	↓ losartan concentration		Seek alternative agent (i.e., valsartan) that is not a CYP2C9 substrate. If concomitant therapy is necessary, monitor for diminished therapeutic effects and/or need for losartan dose increase.	
Calcium Channe						
Verapamil; Diltiazem	Additive clinical effect	Crizotinib	Additive bradycardia	Avoid using the combination of ceritinib with non-dihydropyrimidine calcium channel blockers. If concomitant use is necessary and symptomatic bradycardia occurs, hold ceritinib, adjust or discontinue the calcium channel blocker, and upon recovery resume ceritinib at a reduced dose with frequent monitoring of heart rate.‡ Monitor blood pressure and heart rate regularly. Dose		
					cion of one of the agents may be difficant bradycardia occurs.‡	
Diltiazem; verapamil	CYP3A4 inhibition (moderate)	Bosutinib Doxorubicin	↑ chemotherapy drug concentration	Notify cardiologist/ prescriber to switch to alternative therapy. If concomitant therapy	Avoid co-administration.‡ Consider alternative agent during bosutinib therapy that does not inhibit CYP3A4. Concomitant use should be	
		Imatinib Ivosidenib Neratinib Nilotinib		is necessary, monitor closely for toxicities.	avoided if possible. Consider alternative agent during chemotherapy that does not inhibit CYP3A4.	
		Abemaciclib		If concomitant therapy is necessary, consider reducing the dose by 50 mg increments. Monitor closely for toxicities.	If concomitant therapy is necessary and drug-drug interaction involves QT-prolonging chemotherapy drug, ensure appropriate ECG and	
		Acalabrutinib		If concomitant therapy is necessary, dose reduction of acalabrutinib to 100 mg daily is advised. Monitor closely for toxicities.	electrolyte monitoring.	
		Cobimetinib		If concurrent short- term use (≤14 days) cannot be avoided, reduce cobimetinib to 20 mg daily.		
		Encorafenib		If concomitant therapy is necessary, dose reduction of encorafenib to one-half is advised. Monitor		

				closely for toxicities.	
		Ibrutinib		If concomitant therapy	
		ibratimb		is necessary, dose	
				reduction of ibrutinib	
				to 280 mg daily is	
				advised for B cell	
				malignancies. Monitor	
		01 '1		closely for toxicities.	
		Olaparib		If concomitant therapy	
				is necessary, dose	
				reduction of olaparib	
				tablet to 150 mg twice	
				daily or olaparib	
				capsule to 200 mg	
				twice daily is advised.	
				Monitor closely for	
				toxicities.	
		Sonidegib		If concomitant therapy	
				is necessary, limit	
				concurrent use to less	
				than 14 day and	
				monitor closely for	
				toxicities, especially	
				musculoskeletal.	
Amlodipine	CYP3A4	Ceritinib	个 amlodipine		Monitor for evidence of
	inhibition	Crizotinib	concentration		increased adverse effects or
	(moderate)	Imatinib			toxicity due to amlodipine.
		Palbociclib			Amlodipine dose reduction may
					be necessary.
	CYP3A4	Idelalisib		Notify cardiologist/	Avoid co-administration.
	inhibition			prescriber to switch to	Consider alternative agent
	(strong)			alternative therapy.	during idelalisib therapy. If
	, 3,			.,	concomitant use is necessary,
					closely monitor for adverse
					effects due to amlodipine (i.e.,
					hypotension, peripheral edema)
Statins					7, 7, 7, 7, 7, 7, 7, 7, 7, 7, 7, 7, 7, 7
All statins	Unknown	Pazopanib	Increased	Monitor aspartate	Exercise caution. Monitor
	(atorvastati	322,000	incidence of	aminotransferase	AST/ALT levels if used
	n- also P-		alanine	(AST)/ALT levels if used	concurrently. Dose reduction,
	gp-		transaminase	concurrently. Consider	interruption, or discontinuation
	inhibitor)		(ALT)	adjusting pazopanib if	of therapy may be necessary.
	i i i i i i i i i i i i i i i i i i i		elevations;	concomitant statin use	Documented interaction is with
			statins may	is absolutely necessary.	simvastatin. Insufficient data are
			enhance	is absolutely fielessary.	available to assess the risk of
			hepatotoxicity of pazopanib		concomitant pazopanib with alternative statins.‡ Atorvastatin
			or pazopariio		should be avoided because it is
					also a P-gp inhibitor.

Inhibition Crizotinib Palbocicilib Palboci	Atorvastatin	CYP3A4	Ceritinib	↑ statin		Monitor AST/ALT and creatine
Antiarrhythmics Antiar	Simvastatin	inhibition	Crizotinib	exposure		
Antiarrhythmics Amiodarone Dronedarone Nilotinib Pacitaxel Parapopanib Vincristine Vinbiastine CYP3A4 Amiodarone Dronedarone Dronedarone CYP3A4 Amiodarone Dronedarone CYP3A4 Amiodarone Dronedarone Dronedarone Nilotinib Pacitaxel Pacapanib Vincristine Vinbiastine CYP3A4 Amiodarone Dronedarone Dronedarone Dronedarone Dronedarone Nilotinib Pacitaxel Pacapanib Vincristine Vinbiastine CYP3A4 Amiodarone Dronedarone Dronedarone Nilotinib Pacitaxel Pacapanib Vincristine Vinbiastine CYP3A4 Amiodarone Dronedarone Nilotinib Pacitaxel Pacapanib Vincristine Vinbiastine Crizotinib (moderate) Dronedarone Nilotinib Pacitaxel Pacapanib Vincristine Vinbiastine Crizotinib (moderate) Dronedarone Nilotinib Pacitaxel Pacapanib Vincristine Vinbiastine Crizotinib (moderate) Dronedarone Nilotinib Pacitaxel Pacapanib Pacapanib Vincristine Vinbiastine Crizotinib (moderate) Dronedarone Nilotinib Pacapanib Vincristine Vinbiastine Crizotinib Aminibition (moderate) Dronedarone Nilotinib Nilotinib Pacapanib Vincristine Vinbiastine Crizotinib Additive concentration Additive concentration Additive bradycardia Additive bradycardia cozurs, hold certinib, adjust or discontinue	Lovastatin	(moderate)	Imatinib	·		may be necessary. May consider
CYP3A4 Idelalisib		,	Palbociclib			· · · ·
CYP3A4 Idelalisib						undergo CYP3A4 metabolism
CYP3A4 inhibition (strong) Antiarrhythmics Amiodarone Dronedarone Dronedarone Amiodarone Dronedarone CYP3A4 (inhibition (moderate) Antiorhythmics Artinib Afatinib Doxorubicin Nitothin Pacificate Pacif						<u>=</u>
Inhibition (strong) Participation (moderate) Pazopanib Vincristine Vinblastine Vinblastine Pazopanib Vincredarone Vinblastine Vi						
Antiarrhythmics		CYP3A4	Idelalisib	↑ statin	Notify cardiologist/	Avoid co-administration.
Antiarrhythmics Amiodarone Dronedarone P-g- Inhibition (moderate) P-garapanib Vincristine Vinblastine Amiodarone Dronedarone CYP3A4 Dronedarone Dronedarone Dronedarone Dronedarone CYP3A4 Dronedarone Dro		inhibition		exposure;	prescriber to switch to	Consider alternative statin that
Antiarrhythmics Amiodarone Dronedarone Dr		(strong)		increased risk	alternative statin	does not undergo CYP3A4
Antiarrhythmics P-gp linhibition (moderate) Afatinib Doxorubicin Nilotinib Paclitaxel Pazopanib Vincristine Urinbilastine Dronedarone Amiodarone Amiodarone Doxorubicin Nilotinib Paclitaxel Pazopanib Vincristine Urinbiastine Tornedarone Amiodarone CYP3A4 (moderate) Dronedarone CYP3A4 (inhibition (moderate) Dronedarone Additive Concentration Dronedarone CYP3A4 (inhibition (moderate) Dronedarone Additive Concentration Dronedarone CYP3A4 (inhibition (moderate) Dronedarone CYP3A4 (inhibition (moderate) Dronedarone CYP3A4 (inhibition (moderate) Dronedarone CYP3A4 (inhibition (moderate) Additive Concentration Dronedarone CYP3A4 (inhibition (moderate) Dronedarone CYP3A4 (inhibition (moderate) Additive Concentration CYP3A4 (inhibition (moderate) Dronedarone CYP3A4 (inhibition (moderate) Additive Concentration Dronedarone CYP3A4 (inhibition (moderate) Dronedarone CYP3A4 (inhibition (moderate) Additive Concentration Dronedarone Additive Concentration Dronedarone Additive Concentration Additive Concomitant therapy and inhibition (moderate) Avoid co-administration if recommended action under "Diltazem; verapamil" and individual chemotherapy drug. Avoid using the combination of ceritinib with digoxin. If concomitant use is necessary and symptomatic bradycardia occurs, hold ceritinib, adjust or discontinue				of myopathy	therapy.	metabolism (i.e., pravastatin)
Amiodarone Dronedarone Inhibition (moderate) Doxorubicin Nilotinib Paclitaxel Pazopanib Vincristine Vinblastine Amiodarone Dronedarone Tonedarone Amiodarone Dronedarone Amiodarone Dronedarone Amiodarone Dronedarone Amiodarone Dronedarone Tonedarone Dronedarone Amiodarone Dronedarone Amiodarone Dronedarone Tonedarone Inhibition (moderate) Dronedarone Inhibition (moderate) Dronedarone Droned				and		during idelalisib therapy.
P-gp				rhabdomyolysis		
Dronedarone Inhibition (moderate)	Antiarrhythmics					
Amiodarone Dronedarone Dronedarone Dronedarone CYP3A4 inhibition (moderate) Dronedarone CYP3A4 inhibition (moderate) Dronedarone Dronedaro	Amiodarone	P-gp	Brentuximab	-	If concomitant therapy	Consider alternative
Amiodarone Dronedarone Droneda	Dronedarone	inhibition		chemotherapy	is necessary, monitor	antiarrhythmic agent if possible.
Afatinib Additive clinical effect Afatinib Additive clinical effect Afatinib Avoid co-administration if not were effects of chemotherapy drug if concomitant therapy in necessary. Awoid co-administration if possible. Consider alternative antiarrhythmic antiarrhythmic antiarrhythmic demotherapy that does not inhibit P-gp. If concomitant therapy in necessary and drug-drug interaction involves QT-prolonging chemotherapy drug, ensure appropriate ECG and electrolyte monitoring. Amiodarone CYP3A4 inhibition (moderate) Additive Cobimetriab Cobimetriab Additive Clinical effect Additive Clinical effect Additive Concomitant use is necessary and symptomatic bradycardia occurs, hold ceritinib, adjust or discontinue		(moderate)		drug	for adverse effects of	
Doxorubicin Nilotinib Paclitaxel Pazopanib Vincristine Vinblastine Palbocicilib				concentration	brentuximab.	
Doxorubicin Nilotinib Paclitaxel Pazopanib Vincristine Vinblastine Amiodarone Dronedarone Dronedarone Dronedarone CYP3A4 inhibition (moderate) Dronedarone Droned			Afatinib		Monitor for adverse	
Doxorubicin Doxorubicin Doxorubicin Doxorubicin Doxorubicin Doxorubicin Doxorubicin Doxorubicin Nilotinib Paclitaxel Pazopanib Vincristine Vinblastine Vinblastine Dronedarone CYP3A4 Inhibition (moderate) Imatinib (moderate) Dronedarone CyP3A4 Inhibition (moderate) Dronedarone Dronedarone Dronedarone Cipical (moderate) Dronedarone Dronedarone Dronedarone Cipical (moderate) Dronedarone D					effects of afatinib. If	
Doxorubicin Nilotinib Pazopanib Vincristine Vinblastine Pazopanib Vincristine Vinblastine Vinblastine Vinblastine Pazopanib Vincristine Vinblastine Vinblastine Vinblastine Vinblastine Pazopanib Vincristine Vinblastine Vinblast					not well-tolerated,	
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Vincristine Vinblastine V			Paclitaxel		chemotherapy drug if	antiarrhythmic agent during
Vinblastine			Pazopanib		concomitant therapy	chemotherapy that does not
Amiodarone CYP3A4 Ceritinib Aminibition Cobimetinib Industrial Concentration CYP3A4 Inhibition Cobimetinib Inhibition Cobimetinib Inhibition Comparation Inhibition Cobimetinib Inhibition Comparation Inhibition Cobimetinib Inhibition Comparation Inhibition Cobimetinib Inhibition			Vincristine		necessary.	inhibit P-gp.
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Dronedarone						necessary and drug-drug
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Amiodarone Dronedarone Dronedarone Dronedarone CYP3A4 inhibition (moderate) Dronedarone Cobimetinib Cobimetinib Ibrutinib Concentration						prolonging chemotherapy drug,
Amiodarone Dronedarone CYP3A4 inhibition (moderate) Dronedarone Avoid co-administration if possible. Consider alternative agent during chemotherapy that does not inhibit CYP3A4. Avoid using the combination of ceritinib with digoxin. If concomitant use is necessary and symptomatic bradycardia occurs, hold ceritinib, adjust or discontinue						ensure appropriate ECG and
Dronedarone inhibition (moderate) Imatinib Imatini						electrolyte monitoring.
(moderate)	Amiodarone	CYP3A4	Ceritinib	↑		Monitor for increased adverse
Dronedarone CYP3A4 inhibition (moderate) Bosutinib Cobimetinib (moderate) ↑ Chemotherapy drug See above recommended action under "Diltiazem; agent during chemotherapy that does not inhibit CYP3A4. Digoxin Additive clinical effect Ceritinib Additive bradycardia Avoid using the combination of ceritinib, adjust or discontinue	Dronedarone	inhibition	Crizotinib	antiarrhythmic		effects or toxicity due to
Dronedarone CYP3A4 inhibition (moderate) Digoxin CYP3A4 inhibition (moderate) Cobimetinib Ibrutinib Concentration Concentration Concentration Verapamil" and individual chemotherapy drug. Additive Colinical Effect Ceritinib Additive Concomitant use is necessary and symptomatic Dradycardia Concomitant use is necessary and symptomatic Dradycardia occurs, hold ceritinib, adjust or discontinue		(moderate)	Imatinib	drug		amiodarone or dronedarone.
Dronedarone CYP3A4 inhibition (moderate) Digoxin CYP3A4 inhibition (moderate) Cobimetinib Ibrutinib Cobimetinib Ibrutinib Cobimetinib Ibrutinib Cobimetinib Ibrutinib Cobimetinib Ibrutinib Cobimetinib Ibrutinib Concentration Concentration Concentration Additive Concentration Additive Colinical Effect Additive Concomitant use is necessary and symptomatic			Palbociclib	concentration		Dose reduction may be
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Concentration concentration verapamil" and individual chemotherapy drug. Digoxin Additive clinical effect concomitant use is necessary and symptomatic bradycardia occurs, hold ceritinib, adjust or discontinue		inhibition	Cobimetinib	chemotherapy	recommended action	possible. Consider alternative
Digoxin Additive clinical effect Additive bradycardia individual chemotherapy drug. Avoid using the combination of ceritinib with digoxin. If concomitant use is necessary and symptomatic bradycardia occurs, hold ceritinib, adjust or discontinue		(moderate)	Ibrutinib	drug	under "Diltiazem;	agent during chemotherapy that
Digoxin Additive clinical effect Ceritinib Additive bradycardia Ceritinib Additive bradycardia Ceritinib Additive bradycardia Concomitant use is necessary and symptomatic bradycardia occurs, hold ceritinib, adjust or discontinue				concentration	verapamil" and	does not inhibit CYP3A4.
Digoxin Additive clinical effect Additive Additive bradycardia Avoid using the combination of ceritinib with digoxin. If concomitant use is necessary and symptomatic bradycardia occurs, hold ceritinib, adjust or discontinue					individual	
clinical bradycardia concomitant use is necessary and symptomatic bradycardia occurs, hold ceritinib, adjust or discontinue					chemotherapy drug.	
effect bradycardia occurs, hold ceritinib, adjust or discontinue	Digoxin	Additive	Ceritinib		_	-
				bradycardia		
digoxin, and upon recovery resume ceritinib at a reduced		effect			•	-
					digoxin, and upon recove	ry resume ceritinib at a reduced

				dose with frequent monitoring of heart rate.‡		
		Crizotinib		Monitor blood pressure and heart rate regularly. Dose		
				reduction or discontinuation	on of one of the agents may be	
				necessary if clinically significant bradycardia occurs.‡		
	P-gp	Ibrutinib	↑ digoxin drug		Monitor levels and	
	inhibition	Neratinib	concentration		signs/symptoms of digoxin	
		Vandetanib			toxicity closely. Decreased	
					digoxin doses may be required.	
		Vemurafenib			Avoid co-administration if	
					possible. If concomitant use	
					cannot be avoided, consider	
					digoxin dose reduction and	
					monitor levels and	
					signs/symptoms of digoxin	
					toxicity closely.	
Flecainide	CYP2D6	Imatinib	↑ flecainide		Monitor for increased adverse	
	inhibition	Panobinostat	concentration		effects or toxicity due to	
					flecainide.	
Amiodarone	Additive	Moderate risk	Additive QTc	Recommend ECG and electrolyte monitoring. Frequency to		
Dofetilide	clinical	QTc	prolongation	be determined by patient-specific factors and QT-		
Dronedarone	effect	prolongers		prolonging drug risk. Avoid combination of high-risk QT-		
Flecainide		(see Table 4)		prolonging chemotherapy and cardiac drugs (i.e., arsenic		
Sotalol		High risk QTc		and dofetilide).		
		prolongers				
		(see Table 4)				

^{*} Drug in *italics* represents enzyme inhibitor in proposed interaction.

- 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.

[†] Color denotes severity of interaction as follows:

[‡] Package insert recommendation.