CHEMOTHERAPY DRUGS

	BLEOMYCIN	CARBOPLATIN CISPLATIN CYTARABINE	CYCLOPHOSPHAMIDE	DACARBAZINE	DEXAMETHASONE	DOXORUBICIN	GEMCITABINE
INTEGRASE INHIBITORS							
• DOLUTEGRAVIR (Tivicay, Triumeq)	√	√	√	√	√	√	√
• ELVITEGRAVIR/COBICISTAT (Stribild, Genvoya)	√	√	⚠ ↑ Cyclophosphamide	√	⚠ ↑ Dexamethasone, potential for ↓ elvitegravir if chronic dexamethasone; intermittent dexamethasone is OK	⚠ ↑ Antineoplastic and cytotoxic properties	√
• RALTEGRAVIR (Isentress)	√	√	√	√	√	√	√
PROTEASE INHIBITORS							
RITONAVIR (Norvir) or cobicistat-boosted PIs, e.g.: • ATAZANAVIR (Reyataz) • DARUNAVIR (Prezcobix, Prezista) • LOPINAVIR (Kaletra)	√	√	⚠ ↑ Cyclophosphamide	√	⚠ ↑ Dexamethasone, potential for ↓ protease inhibitor if chronic dexamethasone; intermittent dexamethasone is OK	⚠ ↑ Antineoplastic and cytotoxic properties	√

CHEMOTHERAPY DRUGS

	BLEOMYCIN	CARBOPLATIN CISPLATIN CYTARABINE	CYCLOPHOSPHAMIDE	DACARBAZINE	DEXAMETHASONE	DOXORUBICIN	GEMCITABINE
NNRTIs							
• RILPIVIRINE (Complera, Edurant)	√	√	√	√	√ Potential for ↓ rilpivirine if chronic dexamethasone; intermittent dexamethasone is OK	√	√
• EFAVIRENZ (Sustiva, Atripla) • ETRAVIRINE (Intelence) • NEVIRAPINE (Viramune)	√	√	⚠ ↑ Cyclophosphamide neurotoxic metabolite	√	⚠ ↓ Dexamethasone	⚠ ↑ Antineoplastic and cytotoxic properties	√
NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITORS							
• TENOFOVIR DISOPROXIL (Viread, Truvada, Atripla, Complera, Stribild)	√	⚠ ↑ Renal toxicity	√	√	√	√	√

CHEMOTHERAPY DRUGS

	ETOPOSIDE	IFOSPHAMIDE	MELPHALAN, MESNA, METHOTREXATE, MELPHALAN	METHYLPREDNISOLONE, PREDNISONE	PROCARBAZINE	VINCRISTINE, VINBLASTINE
INTEGRASE INHIBITORS						
• DOLUTEGRAVIR (Tivicay, Triumeq)	√	√	√	√	√	√
• ELVITEGRAVIR/COBICISTAT (Stribild, Genvoya)	⚠ ↑ Etoposide	⚠ ↓ Ifosphamide activation	√	⚠ ↑ Steroid	√	⚠ ↑ Vinca alkaloid and risk of toxicity
• RALTEGRAVIR (Isentress)	√	√	√	√	√	√
PROTEASE INHIBITORS						
RITONAVIR (Norvir) or cobicistat-boosted PIs, e.g.: • ATAZANAVIR (Reyataz) • DARUNAVIR (Prezcobix, Prezista) • LOPINAVIR (Kaletra)	⚠ ↑ Etoposide	⚠ ↓ Ifosphamide activation	√	⚠ ↑ Steroid	⚠ Possible ↑ active metabolite with ritonavir boosted PIs	⚠ ↑ Vinca alkaloid and risk of toxicity

CHEMOTHERAPY DRUGS

	ETOPOSIDE	IFOSPHAMIDE	MELPHALAN, MESNA, METHOTREXATE, MELPHALAN	METHYLPREDNISOLONE, PREDNISONE	PROCARBAZINE	VINCRISTINE, VINBLASTINE
NNRTIs						
• RILPIVIRINE (Complera, Edurant)	√	√	√	√	√	√
• EFAVIRENZ (Sustiva, Atripla) • ETRAVIRINE (Intelence) • NEVIRAPINE (Viramune)	⚠ ↓ Etoposide	⚠ ↑ Ifosphamide activation and potentially more neurotoxic metabolites	√	⚠ ↓ Steroid	√	⚠ Potential ↓ vinca alkaloid

CHEMOTHERAPY DRUGS

Mechanism of Drug Interactions, Management and Monitoring

	CYCLOPHOSPHAMIDE		CISPLATIN, CYTARABINE, CARBOPLATIN	DEXAMETHASONE		
MECHANISM OF INTERACTION	Transformation to inactive and possibly toxic metabolites CYP 3A4 Inhibition of CYP3A4 may increase drug availability for hydroxylation route thereby leading to increased efficacy and toxicity of cyclophosphamide Cyp2B6 and CYP2C19 induction by ritonavir may possibly increase the active metabolite	Induction of CYP 3A4 may increase toxic metabolite	Potential additive toxicity with other agents such as tenofovir (renal toxicity)	Possibility of increased dexamethasone levels with CYP3A4 inhibitors	Possibility of decreased levels with CYP3A4 inducers	Induction of CYP3A4 (dexamethasone)
MAIN INTERACTING ARVs	Ritonavir and cobicistat-boosted protease inhibitors and cobicistat-boosted elvitegravir	Efavirenz, etravirine, nevirapine	Tenofovir	Ritonavir and cobicistat-boosted protease inhibitors and cobicistat-boosted elvitegravir	Efavirenz, etravirine, nevirapine	PIs, NNRTIs, elvitegravir/ cobicistat, rilpivirine
MANAGEMENT	Adjust dose or consider replacing antiretrovirals with alternate agents	Adjust dose or consider replacing antiretrovirals with alternate agents	Close monitoring of the renal function or consider replacing tenofovir	No dose adjustment suggested	No dose adjustment suggested	Pulse dosing of dexamethasone is OK. Daily/chronic dexamethasone may decrease antiretroviral drugs and should be avoided if possible
MONITORING	Close monitoring of side effects	Close monitoring of side effects (neurotoxicity)	Close monitoring of the renal function (creatine, urine analysis)	Close monitoring of side effects		

CHEMOTHERAPY DRUGS

Mechanism of Drug Interactions, Management and Monitoring

	DOXORUBICINE		ETOPOSIDE		IFOSPHAMIDE	
MECHANISM OF INTERACTION	Enzyme inhibitors may decrease reduction to free radicals via inhibition of cytochrome P450 which may decrease both antineoplastic and cytotoxic properties; however, they may also increase intracellular accumulation of doxorubicin via inhibition of PgP, which may enhance cytotoxic effects and/or systemic toxicity	Enzyme inductors may increased reduction to free radicals via induction of cytochrome P450 which may increase both antineoplastic and cytotoxic properties	Possibility of increased levels with CYP3A4 inhibitors	Possibility of decreased levels with CYP3A4 inducers	Inhibition of CYP 3A4 may inhibit drug activation	Induction of CYP 3A4 may increase activation of ifosfamide but may also produce more potentially neurotoxic metabolites
MAIN INTERACTING ARVs	Ritonavir and cobicistat-boosted protease inhibitors and cobicistat-boosted elvitegravir	Efavirenz, etravirine, nevirapine	Ritonavir and cobicistat-boosted protease inhibitors and cobicistat-boosted elvitegravir	Éfavirenz, etravirine, névirapine	Ritonavir and cobicistat-boosted protease inhibitors and cobicistat-boosted elvitegravir	Efavirenz, etravirine, nevirapine
MANAGEMENT	Adjust dose or consider replacing antiretrovirals with alternate agents	Adjust dose or consider replacing antiretrovirals with alternate agents	Adjust dose or consider replacing antiretrovirals with alternate agents	Adjust dose or consider replacing antiretrovirals with alternate agents	Adjust dose or consider replacing antiretrovirals with alternate agents	Adjust dose or consider replacing antiretrovirals with alternate agents
MONITORING	Close monitoring efficacy and side effects	Close monitoring efficacy and side effects	Close monitoring of side effects (mucositis, myelosuppression and transaminitis)	Close monitoring of efficacy	Close monitoring of efficacy	Close monitoring of efficacy and side effects (neurotoxicity)

	METHYLPREDNISOLONE, PREDNISONE		PROCARBAZINE	VINBLASTINE, VINCRISTINE	
MECHANISM OF INTERACTION	Possible increased level with CYP3A4 inhibitors	Possible decreased level with CYP3A4 inducers	Possible increase of the metabolite active of procarbazine with ritonavir-boosted PI (CYP2B6, 1A) induction.	Possible increased level with CYP3A4 inhibitors	Possible decreased level with CYP3A4 inducers
MAIN INTERACTING ARVs	Ritonavir- and cobicistat-boosted protease inhibitors and cobicistat-boosted elvitegravir	Efavirenz, etravirine, nevirapine	Ritonavir-boosted protease inhibitors	Ritonavir- and cobicistat-boosted protease inhibitors and cobicistat-boosted elvitegravir	Efavirenz, etravirine, nevirapine
MANAGEMENT	Not well studied. Dose modification could be suggested	Not well studied. Dose modification could be suggested	Not well studied. No dose adjustment suggested	Adjust dose or consider replacing antiretrovirals with alternate agents	Adjust dose or consider replacing antiretrovirals with alternate agents
MONITORING	Close monitoring of corticosteroids side effects	None. Steroid efficacy?	None	Close monitoring of side effects (peripheral and autonomic neuropathy, myelosuppression)	Close monitoring of efficacy

√ No dose adjustment required.

⚠ Use combination with caution. Adjustment in drug dose or frequency, additional/more frequent monitoring, or use of an alternative agent may be required. May wish to consult with a pharmacist knowledgeable in HIV drug interactions.

X Contraindicated/avoid combination.

A MANAGEMENT TOOL FOR HIV DRUG-DRUG INTERACTIONS

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