化療藥物劑量調整--肝腎功能不全病人

C/T	Renal impairment	Hepatic impairment	Comment
Ado-Transtuzumab Emtansine (KADcyla)	No dosage adjustment necessary	No dosage adjustment necessary	Adjust by Infusion-related reaction .6 mg/kg First dose reduction: Reduce dose to 3 mg/kg Second dose reduction: Reduce dose to 2.4 mg/kg Hematologic toxicity by: 1.Grade of thrombocytopenia 2. LVEF 3. Hepatotoxicity
Asparaginase	No adjustment necessary	No adjustment necessary	Systemic degraded
Azacitidine	No adjustment necessary	No adjustment necessary	WBC ≥3.0 x10^9/L, ANC ≥ 1.5 x10^9/L, and platelets ≥ 75.0 x10^9/L (before treatment) ANC (x10^9/L) Platelets 10^9/L) <0.5 <25.0 (50%) 0.5 –1.5 25.-50. (67%) >1.5 >50.0 (100%)
Bendamustine	Ccr>10, No adjustment	AST or ALT 2.5-10X ULN and Total bilirubin 1.5-3: Not recommended	Adjust by Hematologic toxicity and infusion reaction
Bleomycin (IV)	Clcr >50 ml/min: 100% Clcr 40-50 ml/min:	NA	Adjust by Toxicity Pulmonary :

	70% Clcr 30-40 ml/min: 60% Clcr 20-30 ml/min: 55% Clcr 10-20 ml/min: 45% Clcr 5-10 ml/min: 40%		Pulmonary diffusion capacity for carbon monoxide (DL_{CO}) <30% to 35% of baseline: DC
Busulfan (IV)	No adjustment necessary	NA	Risk of hepatic veno-occlusive disease with high doses; dosage adjustment may be needed.
Capecitabine (PO)	Clcr 30-50 ml/min: 75% Clcr < 30 ml/min: avoid	NA	Adjust by Hepatotoxicity during treatment
Carboplatin (IV)	Clcr > 60 ml/min Clcr 41-59 ml/min: 250 mg/m^2 Clcr 16-40 ml/min: 200 mg/m^2 HD: target AUCX25, on a non-HD day. Start HD 12-24h after carboplatin administration	Dosage adjustment may not be needed	Adjust subsequent doses based on bone marrow toxicity
Chlorambucil	CrCl 10-50 mL/minute: 75% CrCl <10 mL/minute: 50% Peritoneal dialysis (PD): 50%	NA	Adjust by Hematologic toxicity
Cisplatin (IV)	Clcr >60ml/min: Clcr 45-59 ml/min :75% or go on	NA	In normal renal function, repeated courses should not be given until Scr <

	carboplatin Clcr <45 ml/min: go on carboplatin HD: 50% ($25-50 mg/m^2$) every 3-6weeks after HD or on a non-HD day		1.5 mg/dl and/or BUN < 25 mg/dl
Clofarabine	Clcr ≥30ml/min: no dosage adjustment Clcr≤30 ml/min or >60 y/o and Clcr < 60 contraindicated	NA	ANC<500 lasted for ≥4 weeks, reduce 25%
Cyclo-phosphamide (IV; PO)	Clcr < 10 ml/min: 75% HD: 75% after HD	Bilirubin 3.1-5mg/dl or transaminases >3 times ULN: 75% Serum bilirubin >5 mg/mL: Avoid use.	Adjust by Hematologic toxicity
Cytarabine (IV)	<u>High dose: 1-3g/m^2</u> (1) Scr:1.5-1.9mg/dl or an increase from baseline by 0.5 to 1.2 mg/dl: 1gm/m^2 (2) Scr> 2.0 mg/dl or a change in Scr greater than 1.2 mg/dl: reduced dose to 100mg/m^2/day as continuing dose.	Transaminase elevation: 50%	
Dacarbazine (IV)	Clcr 46-60 ml/min: 80% Clcr 31-45 ml/min: 75% Clcr < 30 ml/min: 70%	NA	May cause hepatotoxicity; monitor closely for signs of toxicity
Dactinomycin (IV)	No adjustment	Any transaminase	

	necessary	increase: 50%	
Daunorubicin (IV)	Scr > 3 mg/dl: 50% Cl <30 mL/minute: 50%	Bilirubin 1.2-3 mg/dl: 75% Bilirubin 3.1-5 mg/dl: 50% Bilirubin > 5 mg/dl: avoid	
Docetaxel (IV)	No adjustment necessary HD: No adjustment necessary, given before or after HD	Bilirubin > ULN: avoid AST/ALT > 1.5 x ULN + ALP >2.5 x ULN: avoid Hepatic impairment dosing adjustment specific for gastric or head and neck cancer: AST/ALT >2.5 to ≤5 x ULN and alkaline phosphatase ≤2.5 x ULN: 80% of dose AST/ALT >1.5 to ≤5 x ULN and alkaline phosphatase >2.5 to ≤5 x ULN: 80% of dose AST/ALT >5 x ULN and/or alkaline phosphatase >5 x ULN: DC	Adjust by Mucositis/ diarrhea/hematological
Doxorubicin (IV)	rNo adjustment necessary HD: No adjustment necessary, after HD or on a non-HD	AST (2-3 x ULN): 75% Bilirubin 1.2-3 mg/dl or AST (>3 x ULN) : 50% Bilirubin 3.1-5 mg/dl: 25% Bilirubin > 5 mg/dl:	

		avoid	
Doxorubicin, liposomal (IV)	NA	Bilirubin 1.2-3 mg/dl: 75% Bilirubin >3.1mg/dl: 50%	Adjust by grade of 1. Hand-foot syndrome 2. Stomatitis 3. Hematologic
Epirubicin (IV)	Scr > 5mg/dl: lower doses HD: No adjustment necessary after HD or on a non-HD day	Bilirubin 1.2-3 mg/dl or AST 2- 4 x ULN: 50% Bilirubin >3 mg/dl or AST > 4 x ULN: 25%	
Eribulin	Ccr 15-49 : 1.1mg/m2 ESRD: avoid	Child-Pugh Class A :1.1mg/m2 Child-Pugh class B : 0.7mg/m2 Child-Pugh class C : avoid	Adjust by ANC/PLT Nonheatologic toxicity
Etoposide (IV; PO)	Clcr 15-50 ml/min: 75% Clcr <15 ml/min: further dose reduction HD: 50% (25-75mg/m^2) before or after HD	Bilirubin 1.5-3 mg/dl or AST 60-180 IU: 50% Bilirubin 3-5 mg/dl: 25% Bilirubin > 5 mg/dl: omit dose	Adjust by Hematologic toxicity
Fludarabine (IV)	Clcr 10-50 ml/min: 75% Clcr < 10 ml/min: 50%	NA	
Fluorouracil (IV)	Extreme caution should be used in pts with renal impairment HD: as usual dose after HD on HD day	Bilirubin > 5mg/dl: avoid	
Gemcitabine (IV)	No adjustment	No adjustment	

	necessary HD: No adjustment necessary. Start HD 6-12h after gemcitabine administeration	necessary Bilirubin >1.6mg/dl : 800mg/m^2	
Hydroxyurea (PO)	Clcr 10-60 ml/min: 50% Clcr < 10 ml/min: 20%	NA	Closely monitoring for bone marrow toxicity in pts with hepatic impairment
Idarubicin (IV)	Clcr 10-50 ml/min:75% Clcr < 10 ml/min: 50%	Bilirubin 2.6-5 mg/dl: 50% Bilirubin > 5 mg/dl: avoid	Adjust by Severe mucositis
Ifosfamide (IV)	Clcr < 10ml/min: 75%	Bilirubin > 3 mg/dl: 25%	
Irinotecan (IV)	N/A Use with caution. HD: 50mg/m^2 weekly, given after HD or on a non-HD day	Bilirubin 1.5-3: 75%	Adjust by ANC, diarrhea, nonhamatologic toxicity
Ixabepilone (IV)	NA	1 AST or ALT ≤ 10 x ULN and bilirubin ≤ 1.5 x ULN: 32 mg/m^2 (3). AST or ALT ≤ 10 x ULN and bilirubin > 1.5- ≤ 3 x ULN: initial 20 mg/m^2, escalate up to max. 30 mg/m^2 in subsequent cycles (4). AST or ALT > 10 x ULN or bilirubin > 3 x ULN: avoid 2. Combination with capecitabine:	Adjust by ANC/ PLT/neuropathy

		(1) AST or ALT > 2.5 x ULN or bilirubin > 1 x ULN: avoid	
Melphalan (IV, PO)	BUN > 30 mg/dl or Scr > 1.5 mg/dl: 50% Clcr 10-50 ml/min: 75% Clcr < 10 ml/min: 50%	NA	By plasma hydrolysis
Methotrexate (IV)(PO)	Clcr 10-50 ml/min: 50% Clcr < 10 ml/min: avoid High dose MTX for ALL Cr 1.5-2 mg/dl: 75% Cr> 2mg/dl : 50%	Bilirubin 3.1-5 mg/dl or AST > 180 IU: 75% Bilirubin > 5mg/dl: avoid	Recue by leucovorin
Mitomycin (IV)	Clcr < 10 ml/min: 75%	NA	Adjust by ANC/PLT
Mitoxantrone (IV)	NA	NA	Do not use in multiple sclerosis pts with abnormal liver function
Oxaliplatin (IV)	Clcr <30 ml/min: reduce dose from 85mg/m^2 to 65mg/m^2	No adjustment necessary	Adjust by ANC/PLT/GI toxicity
Paclitaxel (IV)	No adjustment necessary HD: No adjustment necessary, given before or after HD	175 mg/m^2 3 hrs infusion protocol: (1). Bilirubin ≤ 1.25 x ULN + transaminase < 10 x ULN: 175 mg/m^2 (2). Bilirubin 1.26-2 x ULN + transaminase < 10 x ULN: 135 mg/m^2 (3). Bilirubin 2.01-5 x ULN + transaminase <	Adjust by ANC/PLT

		10 x ULN: 90 mg/m^2 (4). Bilirubin > 5x ULN or transaminase ≥ 10 x ULN: avoid	
Pemetrexed (IV)	Clcr < 45 ml/min: avoid	GOT/GPT >5.1 x ULN): 75%	Adjust by ANC/PLT/ mcositis/ diarrhea/ neutotoxicity
Tegafur & Uracil (PO) UFT	NA	NA	Adjust by ANC/PLT/nonhematologic toxicity
Temozolomide (PO)	NA	NA	
Topotecan (IV)	Clcr > 50 ml/min: 75% Clcr 10-50 ml/min: 50% Clcr < 10 ml/min: 25%	Bilirubin 1.7-15 mg/dl no need adjustment	
Vinblastine (IV) Vincristine (IV)	No adjustment necessary	Bilirubin 1.5-3 mg/dl or AST 60-180 IU: 50% Bilirubin >3 : avoid	
Vinorelbine (IV)	No adjustment necessary HD: 20mg/m^2/week after HD or on a non-HD day	Bilirubin 2.1-3 mg/dl: 50% Bilirubin > 3 mg/dl: 25%	

NA: 指沒有資料或無定論，暫且不用調整。

Monoclonal antibody

C/T	**Renal impairment**	**Hepatic impairment**	**Comment** (check with details)
Bevacizumab (IV)	No dosage adjustment	No dosage adjustment	
Brentuximab	Ccr< 30 ml/min :	Child-Pugh class	Adjust by hematologic toxicity

(IV)	avoid	A :1.2mg/kg Child-Pugh class B,C :avoid	
Cetuximab (IV)	No	No	Adjust by toxicity
Rituximab (IV)	No	No	
Trastuzumab (IV)	No	No	Adjust by LVEF (left ventricular ejection fraction)
Ipilimumab (IV)	No	No	Adjust by liver function during treatment and toxicity
Nivolumab	No	No	Adjust by Cr, liver function, toxicity
Pembrolizumab	No	No	Adjust by Cr, liver function, toxicity

Tyrosin kinase inhibitors

C/T	Renal impairment	Hepatic impairment	Comment
Afatinib	CrCl <30 mL/minute closely monitor and adjust dose if necessary.	(Child-Pugh class A, B, C)：no adjustment	Hepatotoxicity during treatment：withhold until to baseline, 10mg /day less than previous dose
Axitinib (PO)	CrCl 15 -89 mL/minute): No adjustment necessary.	(Child-Pugh class A)：no adjustment (Child-Pugh class B)：50%	1.Adjust by hypertension : 5 mg BID→3 mg BID Persistent hypertension 2. Despite anti-hypertensive therapy：2 mg BID 3. Severe and persistent hypertension despite anti-hypertensive therapy and dose reduction：DC

			2. Cardiac failure 3. hemorrhage 4. Proteinuria
Crizotinib	Ccr< 30ml/min : 250mg qd	No	Adjust by hepatotoxicity
Dasatinib (PO)	NA	No adjustment necessary	Adjust by ANC/PLT /nonhematologic toxicity
Erlotinib (PO)	NA	AST>3 x ULN or direct bilirubin 1-7mg/dl : 75mg	Adjust by liver function/ toxicity (skin, GI) 1. 病人原本肝功能正常:用藥後, total bilirubin 升高值為正常的 3 倍或 GOT/GPT 升高為正常的 5 倍: 停藥. 2. 病人原本肝功能不全: total bilirubin > 3 x ULN: 小心使用; 肝功能有惡化情形時，考慮停藥或減量。 3. 如 total bilirubin 增加兩倍或 GOT/GPT 增加 3 倍: 停藥.
Gefitinib (PO)	No adjustment necessary	No adjustment necessary	Adjust by pulmonary symptom, diarrhea, ocular
Imatinib (PO)	Clcr 40-59 ml/min: Max. 600mg Clcr 20-39 ml/min: start with 50%, max. 400mg Clcr ≤ 20 ml/min: use with caution	severe hepatic impairment: reduce dose by 25%	(During therapy) Bilirubin > 3 x ULN or tansaminase > 5 x ULN: postpone until bilirubin < 1.5 x ULN or tansaminase < 2.5 x ULN Resume treatment at a reduced dose: Adult: 400→300mg, 600→400mg, 800→600mg

			Children: 260→200mg, 340→260mg
Lapatinib (PO)	NA	750mg once daily for Child- Pugh class C	Adjust by cardiotoxicity, dermatologic toxicity, diarrhea, other
Nilotinib (PO)	NA	Newly diagnosed Phila- delphia chromosome (+) CML -chronic phase : 200 mg bid for Child-Pugh class A , B, C. Resistant or intolerant Philadelphia chromosome (+) CML -chronic or accelerated phase : 300mg bid for mild impairment (Child-Pugh class A, B), 200mg for Child-Pugh class C	Dosage Adjustment During Therapy a) For bilirubin >3 x ULN, or ALT or AST> 5 x ULN : withhold . b) Nilotinib may be resumed at a dose of 400 mg once daily if bilitubin<1.5 x ULN, or ALT or AST< 2.5 x ULN.
Pazopanib	No	Bilirubin 1.5-3 : 200mg qd Bilirubin > 3x ULN with ALT level : avoid	Adjust by liver function, toxicity (hypertension, proteinuria, infection)
Rogorafenib	No adjustment	Child-Pugh Class A, B : no dosage adjustment Child-Pugh Class C: avoid	Adjust by liver function/ dermatologic, hypertension/, GI toxicity
Sorafenib (PO)	CCr 20-39 ml/min: 200mg q12 Ccr<20ml/min: not defined	Bilirubin > 1.5 to 3 x ULN : 200mg q12 Bilirubin >3 to 10 x ULN : 200mg every 3 days	Adjust by cardiovascular, GI, dermatologic toxicity

		Albumin<2.5 g/dl: 200mg qd	
Sunitinib (PO)	NA	No adjustment necessary in mild-moderate impairment (Child-Pugh Class A or B)	Adjust by liver function/ LVEF/hypertension/Cr/proteinuria /Dermatologic toxicity
ZIV-Aflibercept	No dosage adjustment	N/A	Adjust by toxicity (GI/hypertension/proteinuria

NA: 指沒有資料或無定論，暫且不用調整。

Proteasome inhibitor

C/T	Renal impairment	Hepatic impairment	Comment
Bortezomib (IV)	No adjustment necessary	Bilirubin > 1.5-3 x ULN: reduce initial dose to 0.7 mg/m^2 in the first cycle, may consider dose escalation to 1 mg/m^2 or reduction to 0.5 mg/m^2 in subsequent cycles	Adjust by ANC/PLT/neuropathic pain

mTOR inhibitor

C/T	Renal impairment	Hepatic impairment	Comment
Everolimus	No adjustment	Child-Pugh class A : 7.5mg qd Child-Pugh class B : 5mg qd Child-Pugh class C : 2.5mg qd	Adjust by toxicity (metabolic, stomatitis, noninfectious pneumonitis)
Tacrolimus (PO)	Use lower end of the dosing range	Use lower end of the dosing range	

Temsirolimus	No	Bilirubin>1-1.5 x ULN or AST > ULN : 15mg weekly Bilirubin >1.5 x ULN :avoid	Adjust by ANC/PLT/nonhematologic toxicity

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3. Annals of Oncology 21: 1395–1403, 2010. Proposal for dosage adjustment and timing of chemotherapy in hemodialyzed patients