

Table S1. Summary of the exemplified cytotoxic drugs. Possible oncologic indications, common dosage, PK parameters and examples of treatment regimens and co-medications are presented for methotrexate, busulfan, etoposide, 5-fluorouracil, cyclophosphamide and ifosfamide. ALL: acute lymphoblastic leukemia; HSCT: hematopoietic stem cell transplant; AML: acute myeloid leukemia; AUC: area under the curve; C_{ss}: concentration at steady state; i.v.: intravenous; p.o.: *per os*/oral.

Compound	Oncologic indications	Common dosage	Half-life t _{1/2}	CL	PK target	Sub-exposure	Over-exposure	Examples of treatment regimens and oncologic co-medications
METHOTREXATE	ALL, meningeal leukemia, breast cancer, mycosis fungoides, lung cancer, non-Hodgkin lymphoma	30-50 mg/m ² bolus i.v. once per week; 15 mg/m ² bolus i.v. 5 days every 2-3 weeks 150 mg/m ² bolus i.v. every 2-3 weeks; 240 mg/m ² i.v. (20min) every 4-7 days; 500-1000 mg/m ² i.v. (36-48h) every 2-3 weeks High dose: 1000-12000 mg/m ² i.v. (1-24h) every 1-3 weeks [1]	8-15 h [1]	4.2-21 L/h/m ² [2] 40-400 mL/min [3] 12 L/h [1]	Mean peak serum threshold at 1000 µmol/L (< 1500 µmol/L) after 6-hour infusion in high-dose regimen [4] Serum level maintained at 700 µmol/L [5] C _{ss} 16-40 µmol/L for 24-hour infusion in children with ALL [6]	Treatment non-efficacy	Acute kidney injury, myelosuppression, mucositis, dermatological side effects, hepatotoxicity [7]	Leucovorin (folinic acid) 5-Fluorouracil Cyclophosphamide Vincristine MIED : methotrexate, ifosfamide, etoposide and dexamethasone [8]
BUSULFAN	Conditioning regimen prior to HSCT	2-hour i.v. infusion of 0.8mg/kg every 6 hours for 4 days [9]	Adult: 2.8-3.9 h [9] Pediatric: 2.24-2.5 h [9]	0.22 L/h/kg [10] Adult: 2.25-2.74 ml/min/kg [9] Pediatric: 2.52-3.97 ml/min/kg [9]	AUC _{cum} 78-101 mg·h/L [11]	Graft failure, relapse [11]	Veno-occlusive disease, graft-versus-host disease, mucositis, transplantation-related mortality [11]	BuCy/CyBu: busulfan, cyclophosphamide [12] Fludarabine Thiotepa Melphalan

ETOPOSIDE	Hodgkin and non-Hodgkin lymphoma, testicular cancer, lung cancer, gastrointestinal cancer, breast cancer, pre-HSCT regimen, hepatocellular carcinoma	50-100 mg/m ² i.v. on days 1-5 or 100 mg/m ² i.v. on days 1, 3 and 5 of a 3-4 weeks treatment cycle [13]	Terminal: 3-12 h [13]	18.5 mL/min [14]	AUC 4.6-8.2 mg·min/mL [15]	Treatment non-efficacy	Myelosuppression [16], palmar erythema [17]	BEAM: carmustine, etoposide, cytarabine, melphalan [18] ICE: ifosfamide, carboplatin, etoposide [19] EPOCH: etoposide, cyclophosphamide, doxorubicin, vincristine, prednisone [20] AVI: doxorubicin, etoposide, ifosfamide [21] Cisplatin Bleomycin MIED : methotrexate, ifosfamide, etoposide and dexamethasone [8]
5-FLUOROURACIL	Colorectal cancer, head and neck cancer, breast cancer, gastrointestinal cancers, skin cancer (incl. pre-cancerous lesions, topical application)	300-600 mg/m ² slow bolus or 24h i.v. (< 1g/day) [22]	Dose-dependent, 5-20 min [22]	5 L/min [4]	AUC 20-25 mg·h/L [23] AUC 20-30 mg·h/L [24]	Treatment non-efficacy	Diarrhea, vomiting, nausea, neutropenia, pyrexia, pulmonary embolism, thrombocytopenia, leukopenia [25]	LV5FU: leucovorin, 5-FU [26] FOLFOX: leucovorin, 5-FU, oxaliplatin [26] FOLFIRI: leucovorin, 5-FU, irinotecan hydrochloride [26] Bevacizumab Cisplatin Mitomycin-C Streptozocin Doxorubicin Carboplatin Methotrexate Cyclophosphamide
CYCLOPHOSPHAMIDE	Conditioning regimen prior to HSCT, ALL, AML, Hodgkin and non-Hodgkin lymphoma, plasmocytoma, ovarian carcinoma, seminoma,	Continuous treatment: 3-6 mg/kg i.v. daily 50-200 mg/day p.o.; Intermittent treatment: 10-15 mg/kg i.v. at 2-5 days interval; High-dose intermittent	6-9 h [27]	< 2 years old: 46.6 mL/min/m ² [28] Renal CL: 5-11 mL/min [27]	Hydroxy-CPA: AUC >50 µmol/L Carboxyethylphosphoramide mustard: AUC 325±25 µmol/L [29]	Treatment non-efficacy	Urinary tract toxicity, hemorrhagic cystitis, cardiotoxicity, pulmonary toxicity, hepatic veno-occlusive disease [30]	BuCy/CyBu: busulfan, cyclophosphamide [12] CHOP: cyclophosphamide, doxorubicin, vincristine, prednisone (R-CHOP: + rituximab [31] ; EPOCH: + etoposide [20]) [32] CTC: cyclophosphamide, thiotepa, carboplatin [33] 5-Fluorouracil Methotrexate Epirubicin

	breast carcinoma, small cell bronchogenic carcinoma, neuroblastoma, Ewing's sarcoma	treatment: 20-40 mg/kg i.v. every 21 to 28 days [27]						Mesna
IFOSFAMIDE	Hodgkin and non-Hodgkin lymphoma, soft tissue sarcomas, Ewing sarcoma, cervical cancer, lung carcinoma, osteosarcoma, thymic cancer, ovarian cancer	30-60 mg/kg i.v. (0.5-2h) per day for 5 days; 125-200 mg/kg continuous i.v. over 24h [34]	4-7 h [34]	3.6-8.02 L/h depending on the posology [35] Renal CL: 6-22 mL/min [34]	NA	Treatment non-efficacy	Nausea, vomiting, encephalopathy, hemorrhagic cystitis, metabolic acidosis, hepatic necrosis (result of hepatic veno-occlusive disease) [36], Fanconi syndrome [37]	ICE: ifosfamide, carboplatin, etoposide [19] AVI: doxorubicin, etoposide, ifosfamide [38] MAID: doxorubicin, ifosfamide, mesna, dacarbazine [39] AIM: doxorubicin, ifosfamide, mesna [40] MIED : methotrexate, ifosfamide, etoposide and dexamethasone [8] Mesna

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