

Supplementary Online Content

Feijen EAM, Leisenring WM, Stratton KL, et al. Derivation of anthracycline and anthraquinone equivalence ratios to doxorubicin for late-onset cardiotoxicity. *JAMA Oncol*. Published online January 31, 2019. doi:10.1001/jamaoncol.2018.6634

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eReferences

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Toxicity Equivalence Ratios Used by Various Clinical Groups for Assessment of Cardiotoxicity

Group(s) using referenced ratio ^a	Doxorubicin	Daunorubicin	Epirubicin	Idarubicin	Mitoxantrone
Berlin-Frankfurt-Münster (BFM) group ¹	1	1 (ref)	-	5	5
Bristol Royal Hospital for Sick Children ²	1 (ref)	1	1	-	-
Childhood Cancer Survivor Study ³	1 (ref)	1	-	3	-
Children's Oncology Group ⁴	1 (ref)	1 ^b	0.67	5	4
Dutch Childhood Oncology Group LATER ⁵	1 (ref)	1	0.67	-	-
Kyushu University, Fukuoka, Japan ⁶	1 (ref)	1	1	1	1
Sookmyung Women's University, Seoul, Korea ⁷	1 (ref)	0.5	0.5	2	2.2
Taiwan Pediatric Oncology Group ⁸	1 (ref)	-	-	3	2

^a All ratios listed are based on hematologic toxicity equivalence rather than cardiac toxicity with the exception of Sookmyung Women's University (which is based on the ratio proposed by Keefe⁹).

^b Ratio of 1 reported in the current version of the COG guidelines (version 4, October 2013); prior versions used 0.83.

eTable 2. Number of Survivors (%) Exposed to Chest Radiation and One or More Anthracyclines or Anthraquinone, N=28,423

	N (%) ^a					
	Chest radiation	Doxorubicin	Daunorubicin	Epirubicin	Idarubicin	Mitoxantrone
Chest radiation	6,361 (21.2)					
Doxorubicin	2,198 (7.6)	9,330 (34.8)	-	-	-	-
Daunorubicin	738 (2.9)	1,505 (6.0)	4,433 (18.0)	-	-	-
Epirubicin	49 (0.2)	28 (0.1)	6 (0.0)	342 (1.1)	-	-
Idarubicin	70 (0.3)	64 (0.3)	158 (0.8)	1 (0.0)	241 (1.1)	-
Mitoxantrone	83 (0.3)	74 (0.3)	136 (0.5)	19 (0.1)	55 (0.2)	265 (0.9)

^a Percentages may not match numbers, as percentages reflect weighting employed in the Childhood Cancer Survivor Study for patients with acute lymphoblastic leukemia, and exclude any participant with missing dose information.

eTable 3. Equivalence Ratios for Different Agents Relative to Doxorubicin After Excluding Survivors With any Chest Radiation

Exposure	No. clinical cardiomyopathy / No. dose information	Mean ratio (95% CI)	Linear dose-response model ratio (95% CI)
Daunorubicin	47 / 3,648	0.69 (0.39-1.28)	0.53 (0.36-0.72)
Epirubicin	8 / 293	0.86 (0.55-4.03)	0.74 (0.22-1.29)
Idarubicin	4 / 171	Not estimable	Not estimable
Mitoxantrone	18 / 182	22.2 (10.8-47.9) ^a	22.6 (13.0-35.0) ^a

^a Estimates shown account for a multiplication factor of 4

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