Analysis of Secondary Leukemia and Myelodysplastic Syndrome After Chemotherapy for Solid Organ Tumors Using the Food and Drug Administration Adverse Event Reporting System (FAERS)

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SUPPLEMENTS

			Incidence of leukem	ia	
Anticancer drug	Reporting odds rati	o (95% confidence interval)	with the anticancer drug	without the anticancer drug	p value
Cytotoxic agents					
Antimetabolites		1			
Fluorouracil	2.74 (0.65-11.5)	⊢ •	5 / 4,353 (0.11%)	3 / 7,146 (0.04%)	0.150
Capecitabine	0.45 (0.05-3.64)	⊢	1 / 2,783 (0.04%)	7 / 8,716 (0.08%)	0.4395
Tipiracil; trifluridine	N/A		0 / 136 (0.00%)	8 / 11,363 (0.07%)	0.7569
Platinum					
Oxaliplatin	14.18 (1.74-115.3)		7 / 3,805 (0.18%)	1 / 7,694 (0.01%)	0.001
Topoisomerase inhibitor					
Irinotecan	1.73 (0.41-7.25)	⊢	3 / 2,960 (0.10%)	5 / 8,539 (0.06%)	0.4467
Molecular targeted drugs					
VEGF inhibitors					
Bevacizumab	N/A		0 / 3,667 (0.00%)	8 / 7.832 (0.10%)	0.0529
Aflibercept	N/A		0 / 127 (0.00%)		0.764
EGFR inhibitors			(,	,	
Panitumumab	N/A		0 / 1,763 (0.00%)	8 / 9.736 (0.08%)	0.228
Cetuximab	1.00 (0.12-8.13)		1 / 1,438 (0.07%)		0.999
Multikinase inhibitor	(0.12 0.10)	' T '	., ., (0.01 /0)		0.000
Regorafenib	N/A		0 / 769 (0.00%)	8 / 10,730 (0.07%)	0.448
MFK inhibitor					
Trametinib	N/A		0 / 132 (0.00%)	8 / 11,367 (0.07%)	0.760
B-RAF inhibitor				_ , _ , _ (, ,	
Dabrafenib	N/A		0 / 104 (0.00%)	8 / 11,395 (0.07%)	0.786
· -			(,	, == (====,	
	(0.01 0.1 1 10 100			
		Reporting odds ratio			

Figure S2. Reporting odds ratios of leukemia in colorectal cancer. VEGF, vascular endothelial growth factor; EGFR, epidermal growth factor receptor; MEK, mitogen-activated protein kinase; ERK, extracellular signal-regulated kinase

			Incide	ence of myelody	splastic syndrome	
Anticancer drug	Reporting odds ratio (95% confidence interval)		with		without	p value
			the anticancer drug		the anticancer drug	
Cytotoxic agents						
Antimetabolites		1				
Fluorouracil	0.27 (0.03-2.27)	⊢	1 /	4,353 (0.02%)	6 / 7,146 (0.08%)	0.1984
Capecitabine	1.25 (0.24-6.46)	⊢	2 /	2,783 (0.07%)	5 / 8,716 (0.06%)	0.7872
Tipiracil; trifluridine	N/A		0 /	136 (0.00%)	7 / 11,363 (0.06%)	0.7722
Platinum						
Oxaliplatin	2.70 (0.60-12.1)	⊢	4 /	3,805 (0.11%)	3 / 7,694 (0.04%)	0.176
Topoisomerase inhibitor						
Irinotecan	N/A		0 /	2,960 (0.00%)	7 / 8,539 (0.08%)	0.1192
Molecular targeted drugs						
VEGE inhibitors						
Bevacizumab	N/A		0 /	3,667 (0.00%)	7 / 7.832 (0.09%)	0.0702
Aflibercept	N/A		0 /	127 (0.00%)	7 / 11,372 (0.06%)	0.779
FGFR inhibitors				121 (0.0070)	7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7	0.770
Panitumumab	N/A		0 /	1.763 (0.00%)	7 / 9.736 (0.07%)	0.260
Cetuximab	N/A		0 /	1.438 (0.00%)	7 / 10,061 (0.07%)	0.3170
Multikinase inhibitor				1,100 (0.0010)		0.0
Regorafenib	N/A		0 /	769 (0.00%)	7 / 10,730 (0.07%)	0.4786
MFK inhibitor			0,	(0.0070)	1 / 10,100 (0.01 /0)	0.110
Trametinib	N/A		0 /	132 (0.00%)	7 / 11,367 (0.06%)	0.775
B-RAF inhibitor			0,	(0.0070)	, _ 37 (0.0070)	3.110
Dabrafenib	N/A		0 /	104 (0.00%)	7 / 11,395 (0.06%)	0.800
Dabraromo			0,	(0.00,0)	1 / 11,000 (0.0070)	0.000
		0.01 0.1 1 10 100				
		Reporting odds ratio				

Figure S3. Reporting odds ratios of myelodysplastic syndromes in colorectal cancer. VEGF, vascular endothelial growth f actor; EGFR, epidermal growth factor receptor; MEK, mitogen-activated protein kinase; ERK, extracellular signal-regulated kinase

				nce of leukemia			
Anticancer drug	Reporting odds ra	atio (95% confidence interval)	with the ar	nticancer drug	without the anticancer drug		p value
Cytotoxic agents							
Antimetabolites		1					
Capecitabine	0.83 (0.29-2.36)	⊢	5 /	2,295 (0.22%)	12 /	4.571 (0.26%)	0.7254
Fluorouracil	1.57 (0.51-4.83)	· -	4 /	1,125 (0.36%)	13 /	5.741 (0.23%)	0.4256
Gimeracil;oteracil;tegaf		⊢	2/	360 (0.56%)	15 /	6,506 (0.23%)	0.227
Platinums						-, (,	
Cisplatin	0.60 (0.17-2.10)	⊢ •	3 /	1,799 (0.17%)	14 /	5,067 (0.28%)	0.4219
Oxaliplatin	3.38 (1.28-8.89)	⊢	7 /	1,183 (0.59%)	10 /	5,683 (0.18%)	0.008
Taxanes	,			,,,		-,	
Paclitaxel	0.38 (0.05-2.89)	⊢	1/	963 (0.10%)	16 /	5.903 (0.27%)	0.333
Docetaxel	0.65 (0.09-4.88)	→	1/	605 (0.17%)	16 /	6,261 (0.26%)	0.669
Anthracyclines	,			,		-,,	
Epirubicin	N/A		0 /	797 (0.00%)	17 /	6,069 (0.28%)	0.134
Topoisomerase inhibitor							
Irinotecan	2.82 (0.81-9.86)	+	3 /	486 (0.62%)	14 /	6,380 (0.22%)	0.0889
Molecular targeted drugs							
VEGF inhibitors							
Ramucirumab	N/A		0 /	643 (0.00%)	17 /	6,223 (0.27%)	0.184
Bevacizumab	N/A		0 /	535 (0.00%)	17 /	6,331 (0.27%)	0.230
HER inhibitors							
Trastuzumab	0.73 (0.10-5.48)	⊢	1 /	544 (0.18%)	16 /	6,322 (0.25%)	0.755
Immune checkpoint inhib	itors						
Nivolumab	N/A		0 /	449 (0.00%)	17 /	6,417 (0.26%)	0.274
Tyrosine kinase inhibitors							
Imatinib	4.66 (1.33-16.3)	├	3 /	304 (0.99%)	14 /		0.008
Sunitinib	N/A		0 /	106 (0.00%)	17 /	6,760 (0.25%)	0.605
		0.01 0.1 1 10 100 Reporting odds ratio					

Figure S4. Reporting odds ratios for leukemia in gastric cancer. VEGF: vascular endothelial growth factor; HER: human epidermal growth factor receptor

				nce of myelody			
Anticancer drug	Reporting odds ra	itio (95% confidence interval)	with the anticancer drug		without the anticancer drug		p value
			tile ai	ilicancer urug	g the anticancer drug		
Cytotoxic agents							
Antimetabolites		1					
Capecitabine	0.33 (0.04-2.76)	├	1 /	2,295 (0.04%)	6 /		0.2828
Fluorouracil	2.04 (0.40-10.5)	⊢	2 /	1,125 (0.18%)	5 /	5,741 (0.09%)	0.3835
Gimeracil;oteracil;tegafur	13.66 (3.05-61.3)	⊢	3 /	360 (0.83%)	4 /	6,506 (0.06%)	< 0.000
Platinums							
Cisplatin	2.11 (0.47-9.46)	⊢+	3 /	1,799 (0.17%)	4 /	5,067 (0.08%)	0.3160
Oxaliplatin	N/A		0 /	1.183 (0.00%)	7 /	5,683 (0.12%)	0.227
Taxanes				, , ,		, , ,	
Paclitaxel	8.20 (1.83-36.7)		4 /	963 (0.42%)	3 /	5.903 (0.05%)	0.001
Docetaxel	1.73 (0.21-14.4)		1/	605 (0.17%)	6 /	6,261 (0.10%)	0.609
Anthracyclines	1.10 (0.21 11.1)	' -	• /	000 (0:11 /0)	0,	0,201 (0.1070)	0.000
Epirubicin	N/A		0 /	797 (0.00%)	7 /	6,069 (0.12%)	0.337
Topoisomerase inhibitor			0,	757 (0.0070)	• •	0,005 (0.1270)	0.001
Irinotecan	2.19 (0.26-18.2)		1 /	486 (0.21%)	6 /	6,380 (0.09%)	0.4569
milotocan	2.13 (0.20 10.2)	' •	• /	400 (0.2170)	0,	0,000 (0.0570)	0.400.
Molecular targeted drugs							
VEGF inhibitors							
Ramucirumab	1.61 (0.19-13.4)		1/	643 (0.16%)	6 /	6.223 (0.10%)	0.6548
Bevacizumab	N/A	, T	0 /	535 (0.00%)	7/		0.441
HER inhibitors	, , , , ,		0,	333 (0.0070)		0,551 (0.1170)	0.441
Trastuzumab	4.66 (0.90-24.1)		2 /	544 (0.37%)	5 /	6,322 (0.08%)	0.043
Immune checkpoint inhib		-	2 /	344 (0.37%)	3 /	0,322 (0.06%)	0.043
Nivolumab	N/A		0 /	449 (0.00%)	7 /	6,417 (0,11%)	0.483
Tyrosine kinase inhibitor			0 /	449 (0.00%)	, ,	0,417 (0.11%)	0.463
Imatinib	s N/A		0 /	204 (0.000()	7 /	6 560 (0 449()	0.568
Sunitinib	N/A N/A		0 /	304 (0.00%)			0.568
Sumunib	N/A		0 /	106 (0.00%)	7 /	6,760 (0.10%)	0.740.
		0.01 0.1 1 10 100					
		0.01 0.1 1 10 100 Reporting odds ratio					

Figure S5. Reporting odds ratios for myelodysplastic syndrome in gastric cancer. VEGF: vascular endothelial growth factor; HER: human epidermal growth factor receptor

			Incidence of leuken	nia	
Anticancer drug	Reporting odds ra	itio (95% confidence interval)	with	without	p value
			the anticancer drug	the anticancer drug	
Cytotoxic agents					
Antimetabolites					
Gemcitabine	4.59 (1.28-16.5)		11 / 5,498 (0.20%		0.0102
Capecitabine	0.63 (0.08-4.85)	├	1 / 1,337 (0.07%		0.6584
Fluorouracil	N/A		0 / 1,305 (0.00%		0.1985
Gimeracil;oteracil;tegaf	ur <i>N/A</i>		0 / 105 (0.00%) 14 / 12,263 (0.11%)	0.7290
Taxanes					
Paclitaxel	N/A		0 / 1,959 (0.00%) 14 / 10,409 (0.13%)	0.1043
Docetaxel	N/A		0 / 235 (0.00%) 14 / 12,133 (0.12%)	0.6023
Platinums					
Oxaliplatin	N/A		0 / 1,427 (0.00%) 14 / 10,941 (0.13%)	0.1764
Cisplatin	N/A		0 / 315 (0.00%) 14 / 12,053 (0.12%)	0.5450
Topoisomerase inhibitor					
Irinotecan	N/A		0 / 1,098 (0.00%) 14 / 11,270 (0.12%)	0.2426
Other					
Thalidomide	N/A		0 / 108 (0.00%) 14 / 12,260 (0.11%)	0.7253
Molecular targeted drugs					
EGFR inhibitors					
Erlotinib	1.21 (0.38-3.85)	⊢	4 / 3,080 (0.13%		0.7508
Cetuximab	N/A		0 / 240 (0.00%) 14 / 12,128 (0.12%)	0.5984
VEGF inhibitor					
Bevacizumab	N/A		0 / 592 (0.00%) 14 / 11,776 (0.12%)	0.4012
Multikinase inhibitor					
Sunitinib	N/A		0 / 198 (0.00%) 14 / 12,170 (0.12%)	0.6330
Immune checkpoint inhib	oitor				
Nivolumab	N/A		0 / 184 (0.00%) 14 / 12,184 (0.11%)	0.6455
mTOR inhibitor					
Everolimus	N/A		0 / 163 (0.00%) 14 / 12,205 (0.11%)	0.6653
		0.01 0.1 1 10 100			
		Reporting odds ratio			

Figure S6. Reporting odds ratios for leukemia in pancreatic cancer. VEGF, vascular endothelial growth factor; mTOR, mammalian target of rapamycin

			Incidence of myelod		
Anticancer drug	Reporting odds ra	tio (95% confidence interval)	with	without	p value
			the anticancer drug	the anticancer drug	
Cytotoxic agents					
Antimetabolites		1			
Gemcitabine	0.83 (0.23-2.95)	⊢ →	4 / 5,498 (0.07%)	6 / 6,870 (0.09%)	0.7768
Capecitabine	N/A		0 / 1,337 (0.00%)	10 / 11,031 (0.09%)	0.2702
Fluorouracil	2.12 (0.45-10.0)	⊢ → − −	2 / 1.305 (0.15%)	8 / 11.063 (0.07%)	0.3306
Gimeracil:oteracil:teg	afur N/A		0 / 105 (0.00%)	10 / 12.263 (0.08%)	0.7697
Taxanes					
Paclitaxel	1.33 (0.28-6.26)	⊢ ◆ − −	2 / 1.959 (0.10%)	8 / 10.409 (0.08%)	0.7189
Docetaxel	N/A		0 / 235 (0.00%)	10 / 12.133 (0.08%)	0.659
Platinums			(,		0.000
Oxaliplatin	1.92 (0.41-9.04)	⊢	2 / 1.427 (0.14%)	8 / 10.941 (0.07%)	0.402
Cisplatin	16.55 (4.26-64.3)		3 / 315 (0.95%)	7 / 12.053 (0.06%)	<0.000
Topoisomerase inhibito		' - '	37 313 (0.3370)	7 7 12,000 (0.0070)	٦٥.000
Irinotecan	6.86 (1.93-24.4)		4 / 1.098 (0.36%)	6 / 11,270 (0,05%)	0.000
Other	0.00 (1.00 24.4)	' * '	47 1,050 (0.5070)	0711,270 (0.0370)	0.000
Thalidomide	N/A		0 / 108 (0.00%)	10 / 12,260 (0.08%)	0.766
manaomac	, , , , ,		0 / 100 (0.00 /0)	10 / 12,200 (0.0070)	0.7000
Molecular targeted drugs					
FGFR inhibitors	•				
Erlotinib	0.33 (0.04-2.64)		1 / 3,080 (0.03%)	9 / 9.288 (0.10%)	0.2756
Cetuximab	N/A		0 / 240 (0.00%)	10 / 12.128 (0.08%)	0.656
VEGF inhibitor	1000		07 240 (0.00%)	10 / 12,128 (0.08%)	0.030
Bevacizumab	N/A		0 / 592 (0.00%)	10 / 11.776 (0.08%)	0.478
Multikinase inhibitor	IVA		07 592 (0.00%)	10 / 11,776 (0.06%)	0.476
	0.170		0 / 198 (0.00%)	40 (40 470 (0 000))	0.000
Sunitinib	N/A		0 / 198 (0.00%)	10 / 12,170 (0.08%)	0.686
Immune checkpoint inh				10 / 10 101 /0 000/	
Nivolumab	N/A		0 / 184 (0.00%)	10 / 12,184 (0.08%)	0.697
mTOR inhibitor				10 / 10 005 /0 000/	0.744
Everolimus	N/A		0 / 163 (0.00%)	10 / 12,205 (0.08%)	0.714
		0.01 0.1 1 10 100 Reporting odds ratio			

Figure S7. Reporting odds ratios for myelodysplastic syndrome in pancreatic cancer. VEGF, vascular endothelial growth factor; mTOR, mammalian target of rapamycin

					Incidence of myelodysplastic syndrome				
Anticancer drug	Reporting odds ra	with without the anticancer drug the anticancer drug				p value			
Cytotoxic agents									
Topoisomerase inhib	oitors	I							
Étoposide	5.29 (1.14-24.5)	├	9 /	1,671 (0.54%)	2 /	1,954 (0.10%)	0.0173		
Irinotecan	2.14 (0.57-8.11)	⊢	3 /	541 (0.55%)	8 /	3,084 (0.26%)	0.2497		
Topotecan	N/A		0 /	376 (0.00%)	11 /	3,249 (0.34%)	0.2585		
Platinums									
Carboplatin	6.17 (1.64-23.3)		8 /	1,098 (0.73%)	3 /	2,527 (0.12%)	0.0022		
Cisplatin	10.57 (2.28-49.0)	⊢ → − 1	9 /	1,088 (0.83%)	2 /	2,537 (0.08%)	0.0002		
Taxane									
Paclitaxel	30.00 (9.05-99.5)	⊢	6 /	145 (4.14%)	5 /	3,480 (0.14%)	<0.0001		
Molecular targeted dru	ıas								
Immune checkpoint									
Nivolumab .	N/A		0 /	468 (0.00%)	11 /	3,157 (0.35%)	0.2009		
Ipilimumab	N/A		0 /	358 (0.00%)	11 /	3,267 (0.34%)	0.2715		
		0.01 0.1 10 100							
		Reporting odds ratio							

Figure S8. Reporting odds ratios for myelodysplastic syndrome in small cell lung cancer

			Incidence of leuker		
Anticancer drug	Reporting odds rat	io (95% confidence interval)	with the anticancer drug	without the anticancer drug	p value
Cytotoxic agents					
Platinums		1			
Carboplatin	2.97 (1.63-5.42)	⊢ •	18 / 6,992 (0.26%) 26 / 29,938 (0.09%)	0.000
Cisplatin	7.79 (4.30-14.1)	⊢ •→	20 / 3,583 (0.56%) 24 / 33,347 (0.07%)	< 0.000
Antimetabolites					
Pemetrexed	0.72 (0.26-2.03)	⊢ • ⊢	4 / 4.478 (0.09%) 40 / 32.452 (0.12%)	0.5372
Gemcitabine	3.69 (1.86-7.31)	⊢◆	11 / 3,068 (0.36%	33 / 33,862 (0.10%)	<0.000
Taxanes				,	
Paclitaxel	3.22 (1.68-6.15)	⊢•	13 / 4,269 (0.30%) 31 / 32,661 (0.09%)	0.000
Docetaxel	7.05 (3.73-13.3)		14 / 2,305 (0.61%		< 0.000
Vinca alkaloid	1100 (0110 1010)	' - '	2,000 (0.01.0	,	
Vinorelbine	5.13 (2.28-11.5)	→	7 / 1.320 (0.53%) 37 / 35.610 (0.10%)	<0.000
Topoisomerase inhibito		' - '	7 7 1,020 (0.0070) 01 / 00,010 (0.10/0)	-0.000
Etoposide	28.84 (13.8-60.5)	L	9 / 335 (2.69%) 35 / 36.595 (0.10%)	<0.000
Irinotecan	8.12 (1.95-33.8)		2 / 217 (0.92%		0.000
Other	6.12 (1.95-33.6)	-	27 217 (0.92%)	7 42 / 30,713 (0.11%)	5.000
Thalidomide	N/A		0 / 138 (0.00%) 44 / 36,792 (0.12%)	0.684
Molecular targeted drugs EGFR inhibitors					
Erlotinib	0.69 (0.29-1.64)	——	6 / 6.835 (0.09%	38 / 30.095 (0.13%)	0.405
Gefitinib	2.22 (0.88-5.65)		5 / 2.015 (0.25%		0.403
Afatinib	0.55 (0.08-3.99)		1 / 1.501 (0.25%		0.547
Osimertinib	1.18 (0.29-4.89)				0.816
Cetuximab	0.62 (0.08-4.48)	•	1 / 1,341 (0.07%		0.629
Necitumumab	N/A		0 / 151 (0.00%) 44 / 36,779 (0.12%)	0.670
Immune checkpoint inhi			4 / 5 400 /0 000/		0.004
Nivolumab	0.13 (0.02-0.97)	—	1 / 5,463 (0.02%		0.091
Pembrolizumab	N/A		0 / 1,759 (0.00%		0.137
Ipilimumab	N/A		0 / 675 (0.00%		0.365
Atezolizumab	N/A		0 / 660 (0.00%		0.370
Durvalumab	1.64 (0.23-11.9)	⊢	1 / 517 (0.19%) 43 / 36,413 (0.12%)	0.622
VEGF inhibitors					
Bevacizumab	0.20 (0.03-1.47)	⊢	1 / 3,798 (0.03%		0.080
Ramucirumab	N/A		0 / 222 (0.00%) 44 / 36,708 (0.12%)	0.605
ALK inhibitors					
Crizotinib	0.50 (0.07-3.62)		1 / 1.646 (0.06%) 43 / 35,284 (0,12%)	0.4823
Ceritinib	N/A	'	0 / 598 (0.00%) 44 / 36.332 (0.12%)	0.394
Alectinib	N/A		0 / 314 (0.00%		0.538
Triple angiokinase inhib				,	
Nintedanib	N/A		0 / 293 (0.00%) 44 / 36,637 (0.12%)	0.552
Multikinase inhibitors	7477		233 (0.007)	, 447 55,557 (5.1270)	0.002
Sorafenib	N/A		0 / 201 (0.00%) 44 / 36,729 (0.12%)	0.623
Sunitinib	N/A		0 / 167 (0.00%		0.654
B-RAF inhibitor	14/71		37 107 (0.00%)	, 44/30,703 (0.12%)	0.054
	0.170		0 / 170 (0.00%	14 (26 760 (0 400))	0.654
Dabrafenib	N/A		0 / 170 (0.00%) 44 / 36,760 (0.12%)	0.651
MEK inhibitor	0.440		0 / 470 / 0 000	11 / 00 700 /0 100:	0.05
Trametinib	N/A		0 / 170 (0.00%) 44 / 36,760 (0.12%)	0.651
Proteasome inhibitor					
Bortezomib	N/A	l l	0 / 126 (0.00%) 44 / 36,804 (0,12%)	0.697

Figure S9. Reporting odds ratios for leukemia in non-small cell lung cancer. VEGF, vascular endothelial growth factor; ALK, anaplastic lymphoma kinase; MEK, mitogen-activated protein kinase; ERK, extracellular signal-regulated kinase

Anticancer drug	Reporting odds ratio (95% confidence interval)			Incidence of myelodysplastic syndrome with				
Anticancer drug	Reporting odds ratio (tieper and goale rane (ee //e ee macross miles ran)			the anticancer drug	p value		
Cytotoxic agents								
Platinums		i i						
Carboplatin	5.25 (2.81-9.79)		22 /	6,992 (0.31%)	18 / 29,938 (0.06%)	<0.000		
Cisplatin	2.33 (1.07-5.06)	⊢	8 /	3,583 (0.22%)	32 / 33,347 (0.10%)	0.027		
Antimetabolites								
Pemetrexed	0.81 (0.29-2.26)	⊢• ⊢	4 /	4,478 (0.09%)	36 / 32,452 (0.11%)	0.6803		
Gemcitabine	1.95 (0.82-4.65)	 ◆ 	6 /	3,068 (0.20%)	34 / 33,862 (0.10%)	0.1249		
Taxanes								
Paclitaxel	3.69 (1.90-7.16)	⊢ •−	13 /	4,269 (0.30%)	27 / 32,661 (0.08%)	<0.000		
Docetaxel	1.22 (0.38-3.95)	⊢▶	3 /	2,305 (0.13%)	37 / 34,625 (0.11%)	0.7420		
Vinca alkaloid								
Vinorelbine	4.78 (2.00-11.4)	⊢	6 /	1,320 (0.45%)	34 / 35,610 (0.10%)	<0.000		
Topoisomerase inhibit	tors							
Étoposide	23.65 (10.4-53.8)	⊢•⊣	7 /	335 (2.09%)	33 / 36,595 (0.09%)	<0.000		
Irinotecan	4.35 (0.60-31.8)	⊢	1 /	217 (0.46%)	39 / 36,713 (0.11%)	0.113		
Other								
Thalidomide	N/A		0 /	138 (0.00%)	40 / 36,792 (0.11%)	0.698		
Molecular targeted drug	s							
EGFR inhibitors								
Erlotinib	0.36 (0.11-1.16)	⊢ •••	3 /	6,835 (0.04%)	37 / 30,095 (0.12%)	0.072		
Gefitinib	0.91 (0.22-3.78)	⊢	2 /	2,015 (0.10%)	38 / 34,915 (0.11%)	0.898		
Afatinib	N/A		0 /	1,501 (0.00%)	40 / 35,429 (0.11%)	0.192		
Osimertinib	0.64 (0.09-4.63)	⊢	1 /	1,430 (0.07%)	39 / 35,500 (0.11%)	0.203		
Cetuximab	N/A		0 /	1,341 (0.00%)	40 / 35,589 (0.11%)	0.219		
Necitumumab	N/A		0 /	151 (0.00%)	40 / 36,779 (0.11%)	0.685		
Immune checkpoint in	hibitors							
Nivolumab	0.82 (0.32-2.10)	⊢• ⊢	5 /	5,463 (0.09%)	35 / 31,467 (0.11%)	0.682		
Pembrolizumab	2.22 (0.79-6.26)	 	4 /	1,759 (0.23%)	36 / 35,171 (0.10%)	0.119		
Ipilimumab	N/A		0 /	675 (0.00%)	40 / 36,255 (0.11%)	0.387		
Atezolizumab	1.41 (0.19-10.3)	⊢	1 /	660 (0.15%)	39 / 36,270 (0.11%)	0.733		
Durvalumab	N/A	· · · · · ·	0 /	517 (0.00%)	40 / 36,413 (0.11%)	0.450		
VEGF inhibitors								
Bevacizumab	0.46 (0.11-1.90)	⊢	2 /	3,798 (0.05%)	38 / 33,132 (0.11%)	0.271		
Ramucirumab	N/A	· · · ·	0 /	222 (0.00%)	40 / 36,708 (0.11%)	0.622		
ALK inhibitors				, ,				
Crizotinib	N/A		0 /	1.646 (0.00%)	40 / 35,284 (0.11%)	0.171		
Ceritinib	N/A		0 /	598 (0.00%)	40 / 36,332 (0.11%)	0.416		
Alectinib	N/A		0 /	314 (0.00%)	40 / 36.616 (0.11%)	0.557		
Triple angiokinase inh				(/	,			
Nintedanib	N/A		0 /	293 (0.00%)	40 / 36,637 (0.11%)	0.571		
Multikinase inhibitors			0,	200 (0.0070)	107 00,007 (0.1170)	0.011		
Sorafenib	N/A		0 /	201 (0.00%)	40 / 36.729 (0.11%)	0.639		
Sunitinib	N/A		0 /	167 (0.00%)	40 / 36,763 (0.11%)	0.669		
B-RAF inhibitor	, , , ,		0,	101 (0.0070)	107 00,700 (0.1170)	0.000		
Dabrafenib	N/A		0 /	170 (0.00%)	40 / 36,760 (0,11%)	0.667		
MEK inhibitor			0 /	.10 (0.0070)	.57 55,755 (5.1170)	0.007		
Trametinib	N/A		0 /	170 (0.00%)	40 / 36,760 (0.11%)	0.667		
Proteasome inhibitor			0 /	.70 (0.0070)	45 / 50,700 (0.1170)	0.007		
Bortezomib	N/A		0 /	126 (0.00%)	40 / 36,804 (0.11%)	0.711		
	0.0	1 0.1 1 10 100						

Figure S10. Reporting odds ratios for myelodysplastic syndrome in non-small cell lung cancer. VEGF, vascular endothelial growth factor; ALK, anaplastic lymphoma kinase; MEK, mitogen-activated protein kinase; ERK, extracellular signal-regulated kinase

				Incidence of leukemia				
Anticancer drug	Reporting odds ratio	o (95% confidence interval)	with		witho	ut	p value	
			the anticancer drug		the anticancer drug			
Cytotoxic agents								
Platinums		1						
Cisplatin	0.31 (0.07-1.37)	⊢ •−+	2 /	1,198 (0.17%)	12 /	2,211 (0.54%)	0.1014	
Oxaliplatin	2.28 (0.63-8.20)	⊢•	3 /	366 (0.82%)	11 /	3,043 (0.36%)	0.1953	
Carboplatin	0.69 (0.09-5.30)	⊢	1 /	341 (0.29%)	13 /	3,068 (0.42%)	0.7208	
Antimetabolites								
Fluorouracil	4.93 (1.54-15.7)		10 /	1,153 (0.87%)	4 /	2,256 (0.18%)	0.0029	
Capecitabine	1.28 (0.36-4.60)	⊢ •	3 /	600 (0.50%)	11 /	2,809 (0.39%)	0.7063	
Taxanes								
Paclitaxel	N/A		0 /	510 (0.00%)	14 /	2,899 (0.48%)	0.1158	
Docetaxel	N/A		0 /	494 (0.00%)	14 /	2,915 (0.48%)	0.1227	
Topoisomerase inhibitor								
Irinotecan	N/A		0 /	297 (0.00%)	14 /	3,112 (0.45%)	0.2467	
Anthracycline								
Epirubicin	N/A		0 /	148 (0.00%)	14 /	3,261 (0.43%)	0.4244	
Molecular targeted drugs								
EGFR inhibitor								
Cetuximab	N/A		0 /	216 (0.00%)	14 /	3,193 (0.44%)	0.3295	
Erlotinib	N/A		0 /	101 (0.00%)	14 /	3,308 (0.42%)	0.5124	
VEGF inhibitor								
Bevacizumab	N/A		0 /	186 (0.00%)	14 /	3,223 (0.43%)	0.3677	
Immune checkpoint inhib	oitors							
Nivolumab	N/A		0 /	139 (0.00%)	14 /	3,270 (0.43%)	0.4395	
	(0.01 0.1 1 10 100 Reporting odds ratio						

Figure S11. Reporting odds ratios for leukemia in esophageal cancer. EGFR, epidermal growth factor receptor; VEGF, vascular endothelial growth factor

			Incide				
Anticancer drug	Reporting odds ratio (95% confidence interval)		with	p value			
			the anticancer drug		the anticancer drug		
Cytotoxic agents							
Platinums		1					
Cisplatin	1.39 (0.48-4.00)	⊢ •	6 /	1,198 (0.50%)	8 /	2,211 (0.36%)	0.5446
Oxaliplatin	N/A		0 /	366 (0.00%)	14 /	3,043 (0.46%)	0.1935
Carboplatin	0.69 (0.09-5.30)	⊢	1 /	341 (0.29%)	13 /	3,068 (0.42%)	0.7208
Antimetabolites							
Fluorouracil	11.85 (2.65-53.1)	 • 	12 /	1,153 (1.04%)	2 /	2,256 (0.09%)	< 0.0001
Capecitabine	0.36 (0.05-2.75)	⊢	1 /	600 (0.17%)	13 /	2,809 (0.46%)	0.3032
Taxanes							
Paclitaxel	0.44 (0.06-3.34)	⊢	1 /	510 (0.20%)	13 /	2,899 (0.45%)	0.4112
Docetaxel	N/A		0 /	494 (0.00%)	14 /	2,915 (0.48%)	0.1227
Topoisomerase inhibito	r			, ,		, ,	
Irinotecan	0.81 (0.10-6.18)	⊢	1 /	297 (0.34%)	13 /	3,112 (0.42%)	0.8347
Anthracycline							
Epirubicin	N/A		0 /	148 (0.00%)	14 /	3,261 (0.43%)	0.4244
Molecular targeted drugs							
EGFR inhibitor							
Cetuximab	N/A		0 /	216 (0.00%)	14 /	3,193 (0.44%)	0.3295
Erlotinib	N/A		0 /	101 (0.00%)	14 /	3,308 (0.42%)	0.5124
VEGF inhibitor							
Bevacizumab	N/A		0 /	186 (0.00%)	14 /	3,223 (0.43%)	0.3677
Immune checkpoint inh	ibitors						
Nivolumab .	N/A		0 /	139 (0.00%)	14 /	3,270 (0.43%)	0.4395
		0.01 0.1 1 10 100					
		Reporting odds ratio					

Figure S12. Reporting odds ratios for myelodysplastic syndrome in esophageal cancer. EGFR, epidermal growth factor receptor; VEGF, vascular endothelial growth factor

				Incidence of leukemia			
Anticancer drug	Reporting odds ra	itio (95% confidence interval)	with		without	p value	
			the an	ticancer drug	the anticancer drug		
Cytotoxic agents							
Platinums		1					
Cisplatin	2.85 (0.83-9.78)	⊢•	7 /	694 (1.01%)	4 / 1,124 (0.36%)	0.0812	
Carboplatin	4.21 (1.28-13.9)	⊢	6 /	407 (1.47%)	5 / 1,411 (0.35%)	0.0103	
Taxane							
Paclitaxel	2.32 (0.71-7.63)	 	6 /	622 (0.96%)	5 / 1,196 (0.42%)	0.1540	
Antimetabolites							
Fluorouracil	5.27 (1.38-20.1)	├	3 /	123 (2.44%)	8 / 1,695 (0.47%)	0.0066	
Topoisomerase inhibitors	6						
Topotecan	N/A		0 /	102 (0.00%)	11 / 1,716 (0.64%)	0.4173	
Molecular targeted drugs							
VEGF inhibitor							
Bevacizumab	N/A		0 /	432 (0.00%)	11 / 1,386 (0.79%)	0.0633	
		0.01 0.1 1 10 100 Reporting odds ratio					

Figure S13. Reporting odds ratios for leukemia in cervical cancer. VEGF: vascular endothelial growth factor

Anticancer drug	Reporting odds ratio (95% confidence interval)		Incidence of myelodysplastic syndrome with			p value
	reporting odds rado (55% confidence interval)			ticancer drug	the anticancer drug	p value
Cytotoxic agents						
Platinums		1				
Cisplatin	N/A		3 /	694 (0.43%)	0 / 1,124 (0.00%)	0.0274
Carboplatin	N/A		3 /	407 (0.74%)	0 / 1,411 (0.00%)	0.0012
Taxane						
Paclitaxel	N/A		3 /	622 (0.48%)	0 / 1,196 (0.00%)	0.0163
Antimetabolites						
Fluorouracil	28.00 (2.52-311.0)	├	2 /	123 (1.63%)	1 / 1,695 (0.06%)	< 0.0001
Topoisomerase inhibite	ors					
Topotecan	8.49 (0.76-94.4)	+ -	1 /	102 (0.98%)	2 / 1,716 (0.12%)	0.0368
Molecular targeted drugs	3					
VEGF inhibitor						
Bevacizumab	N/A		0 /	432 (0.00%)	3 / 1,386 (0.22%)	0.3332
		0.01 0.1 1 10 100				
		Reporting odds ratio				

Figure S14. Reporting odds ratios for myelodysplastic syndrome in cervical cancer. VEGF: vascular endothelial growth factor