



## Original Article

### **Optimizing Treatment, Minimizing Risk: Therapeutic Drug Monitoring in Hematological Malignancies**

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## **Supplementary Files**

**Supplementary Table 1.** Participant characteristics, institutional profiles, and therapeutic drug monitoring practices in hematology care per TDM availability, TDM performance, TDM turnaround time, and TDM-based modification.

	TDM availability					TDM performance					TDM turnaround time						TDM-based modification									
	No		Yes		p value	Onsite		Outsourced		p value	<1 day		1-3 days		>3 days		p value	No		Yes		At times		p value		
	n	%	n	%		n	%	n	%		n	%	n	%	n	%		n	%	n	%	n	%		n	%
<b>Participant specialty</b>																										
Hematology	4	3.4	114	96.6	1.000	94	79.7	19	16.1	0.711	38	32.2	61	51.7	11	9.3	0.089	0	0.0	84	71.2	30	25.4	0.675		
Oncology	0	0.0	27	100.0	0.598	22	81.5	5	18.5	1.000	11	40.7	13	48.1	2	7.4	0.258	0	0.0	21	77.8	6	22.2	0.694		
Pediatrics	0	0.0	11	100.0	1.000	9	81.8	2	18.2	1.000	4	36.4	5	45.5	2	18.2	0.608	0	0.0	8	72.7	3	27.3	1.000		
Intensive care	0	0.0	5	100.0	1.000	5	100.0	0	0.0	0.588	3	60.0	2	40.0	0	0.0	0.409	0	0.0	3	60.0	2	40.0	0.622		
Internal medicine	0	0.0	36	100.0	0.607	32	88.9	4	11.1	0.338	10	27.8	21	58.3	4	11.1	1.000	1	2.8	29	80.6	6	16.7	0.055		
Pharmacy	0	0.0	4	100.0	1.000	4	100.0	0	0.0	1.000	2	50.0	2	50.0	0	0.0	0.775	0	0.0	4	100.0	0	0.0	0.584		
Infectious diseases	2	4.8	40	95.2	0.630	31	73.8	9	21.4	0.490	3	7.1	31	73.8	6	14.3	<b>0.001</b>	0	0.0	29	69.0	11	26.2	1.000		
Other	1	14.3	6	85.7	0.215	6	85.7	0	0.0	0.594	2	28.6	3	42.9	1	14.3	0.858	0	0.0	4	57.1	2	28.6	0.671		
<b>Institution profile</b>																										
General/Acute care hospital	3	5.2	55	94.8	0.385	45	77.6	8	13.8	<b>0.004</b>	14	24.1	32	55.2	5	8.6	0.566	1	1.7	40	69.0	14	24.1	0.174		
Regional/County hospital	0	0.0	11	100.0		8	72.7	3	27.3		4	36.4	7	63.6	0	0.0		0	0.0	9	81.8	2	18.2			
Specialized hospital	1	3.4	28	96.6		16	55.2	12	41.4		6	20.7	15	51.7	7	24.1		0	0.0	15	51.7	13	44.8			
Teaching hospital	2	2.0	99	98.0		88	87.1	11	10.9		31	30.7	54	53.5	14	13.9		0	0.0	75	74.3	24	23.8			
Outpatient clinic	0	0.0	0	0.0		0	0.0	0	0.0		0	0.0	0	0.0	0	0.0		0	0.0	0	0.0	0	0.0		0	0.0
Other	1	10.0	9	90.0		7	70.0	2	20.0		2	20.0	6	60.0	0	0.0		0	0.0	0	0.0	8	80.0		1	10.0
<b>Institution size</b>																										
<200 beds	1	5.0	19	95.0	0.575	10	50.0	9	45.0	<b>&lt;0.001</b>	5	25.0	10	50.0	4	20.0	0.777	0	0.0	12	60.0	7	35.0	<b>0.002</b>		
200-500 beds	2	3.9	49	96.1		33	64.7	15	29.4		14	27.5	26	51.0	7	13.7		1	2.0	27	52.9	21	41.2			
>500 beds	4	2.9	134	97.1		121	87.7	12	8.7		38	27.5	78	56.5	15	10.9		0	0.0	108	78.3	26	18.8			
<b>Hematology beds</b>																										
0-20 beds	2	3.3	59	96.7	1.000	43	70.5	14	23.0	0.335	17	27.9	33	54.1	6	9.8	0.561	1	1.6	40	65.6	18	29.5	0.556		
21-50 beds	3	3.1	95	96.9		80	81.6	15	15.3		28	28.6	50	51.0	16	16.3		0	0.0	70	71.4	25	25.5			
>51 beds	2	4.0	48	96.0		41	82.0	7	14.0		12	24.0	31	62.0	4	8.0		0	0.0	37	74.0	11	22.0			
<b>Hospital target</b>																										
Adult	5	4.6	103	95.4	0.074	79	73.1	22	20.4	0.128	30	27.8	54	50.0	15	13.9	0.776	0	0.0	72	66.7	31	28.7	0.509		
Children	1	14.3	6	85.7		4	57.1	2	28.6		1	14.3	4	57.1	1	14.3		0	0.0	4	57.1	2	28.6			
Both	1	1.1	93	98.9		81	86.2	12	12.8		26	27.7	56	59.6	10	10.6		1	1.1	71	75.5	21	22.3			
<b>Hematological targets</b>																										
Acute leukemia	7	3.5	191	96.5	1.000	156	78.8	33	16.7	0.421	53	26.8	108	54.5	25	12.6	0.904	1	0.5	137	69.2	53	26.8	0.333		

	TDM availability					TDM performance					TDM turnaround time						TDM-based modification							
	No		Yes		p value	Onsite		Outsourced		p value	<1 day		1-3 days		>3 days		p value	No		Yes		At times		p value
	n	%	n	%		n	%	n	%		n	%	n	%	n	%		n	%	n	%	n	%	
Chronic leukemia	7	3.6	190	96.4	1.000	155	78.7	33	16.8	0.456	54	27.4	106	53.8	25	12.7	0.917	1	0.5	137	69.5	52	26.4	0.549
Lymphoma/Multiple myeloma	7	3.4	199	96.6	1.000	163	79.1	34	16.5	0.084	57	27.7	111	53.9	26	12.6	0.707	1	0.5	144	69.9	54	26.2	0.572
Autologous HSCT	5	2.7	178	97.3	0.211	147	80.3	29	15.8	0.155	49	26.8	101	55.2	23	12.6	0.906	1	0.5	129	70.5	48	26.2	1.000
Allogeneic HSCT	3	2.0	146	98.0	0.106	123	82.6	22	14.8	0.102	42	28.2	84	56.4	17	11.4	0.687	1	0.7	107	71.8	38	25.5	0.802
CAR-T	1	0.9	111	99.1	0.051	98	87.5	13	11.6	<b>0.015</b>	28	25.0	67	59.8	15	13.4	0.487	1	0.9	85	75.9	25	22.3	0.176
<b>Annual hematological inpatients</b>																								
<200 hospitalizations	1	3.3	29	96.7		15	50.0	13	43.3		6	20.0	15	50.0	6	20.0		0	0.0	18	60.0	11	36.7	
201-500 hospitalizations	3	3.8	75	96.2	1.000	63	80.8	11	14.1	<b>&lt;0.001</b>	19	24.4	46	59.0	9	11.5	0.472	0	0.0	53	67.9	22	28.2	0.266
>501 hospitalizations	3	3.0	98	97.0		86	85.1	12	11.9		32	31.7	53	52.5	11	10.9		1	1.0	76	75.2	21	20.8	
<b>TDM found to be beneficial</b>	6	2.9	201	97.1	0.066	163	78.7	36	17.4	1.000	57	27.5	113	54.6	26	12.6	1.000	1	0.5	147	71.0	53	25.6	0.272
<b>TDM availability</b>	0	0.0	202	100.0	-	164	81.2	36	17.8	-	57	28.2	114	56.4	26	12.9	-	1	0.5	147	72.8	54	26.7	-
Onsite	0	0.0	164	100.0	1.000	164	100.0	0	0.0	-	52	31.7	96	58.5	13	7.9	<b>&lt;0.001</b>	1	0.6	128	78.0	35	21.3	<b>0.004</b>
Outsourced	0	0.0	36	100.0		0	0.0	36	100.0	-	5	13.9	18	50.0	13	36.1		0	0.0	19	52.8	17	47.2	
<b>TDM turnaround time</b>																								
Same day	0	0.0	57	100.0		52	91.2	5	8.8		57	100.0	0	0.0	0	0.0		1	1.8	51	89.5	5	8.8	
1-3 days	0	0.0	114	100.0	1.000	96	84.2	18	15.8	<b>&lt;0.001</b>	0	0.0	114	100.0	0	0.0	-	0	0.0	85	74.6	29	25.4	<b>&lt;0.001</b>
>3 days	0	0.0	26	100.0		13	50.0	13	50.0		0	0.0	0	0.0	26	100.0		0	0.0	9	34.6	17	65.4	
<b>Turnaround satisfaction</b>																								
Yes	0	0.0	111	100.0		103	92.8	8	7.2		49	44.1	55	49.5	5	4.5		1	0.9	90	81.1	20	18.0	
No	0	0.0	19	100.0	1.000	8	42.1	11	57.9	<b>&lt;0.001</b>	1	5.3	9	47.4	9	47.4	<b>&lt;0.001</b>	0	0.0	10	52.6	9	47.4	<b>0.006</b>
Not always	0	0.0	70	100.0		52	74.3	16	22.9		7	10.0	48	68.6	12	17.1		0	0.0	45	64.3	25	35.7	
<b>Routine TDM</b>																								
Antineoplastics																								
<i>Busulfan</i>	0	0.0	28	100.0	1.000	24	85.7	4	14.3	0.792	9	32.1	13	46.4	5	17.9	0.460	0	0.0	23	82.1	5	17.9	0.447
<i>Cyclosporin A</i>	0	0.0	168	100.0	1.000	138	82.1	28	16.7	0.338	45	26.8	95	56.5	23	13.7	0.591	0	0.0	123	73.2	45	26.8	0.214
<i>Methotrexate</i>	0	0.0	170	100.0	1.000	138	81.2	30	17.6	1.000	47	27.6	95	55.9	23	13.5	0.857	0	0.0	122	71.8	48	28.2	0.084
Antifungals																								
<i>Isavuconazole</i>	0	0.0	59	100.0	1.000	52	88.1	7	11.9	0.163	8	13.6	40	67.8	11	18.6	<b>0.004</b>	0	0.0	41	69.5	18	30.5	0.637
<i>Itraconazole</i>	0	0.0	33	100.0	1.000	28	84.8	5	15.2	0.806	5	15.2	18	54.5	10	30.3	<b>0.005</b>	0	0.0	18	54.5	15	45.5	<b>0.027</b>
<i>Posaconazole</i>	0	0.0	91	100.0	1.000	76	83.5	15	16.5	0.712	17	18.7	57	62.6	17	18.7	<b>0.005</b>	0	0.0	63	69.2	28	30.8	0.300
<i>Voriconazole</i>	0	0.0	141	100.0	1.000	115	81.6	25	17.7	1.000	30	21.3	85	60.3	24	17.0	<b>&lt;0.001</b>	0	0.0	100	70.9	41	29.1	0.149
<i>Flucytosine</i>	0	0.0	8	100.0	1.000	7	87.5	1	12.5	1.000	1	12.5	5	62.5	2	25.0	0.443	0	0.0	7	87.5	1	12.5	0.697

	TDM availability					TDM performance					TDM turnaround time						TDM-based modification								
	No		Yes		p value	Onsite		Outsourced		p value	<1 day		1-3 days		>3 days		p value	No		Yes		At times		p value	
	n	%	n	%		n	%	n	%		n	%	n	%	n	%		n	%	n	%	n	%		n
Antibiotics																									
<i>Amikacin</i>	0	0.0	121	100.0	1.000	106	87.6	13	10.7	<b>0.002</b>	32	26.4	70	57.9	15	12.4	0.767	0	0.0	93	76.9	28	23.1	0.104	
<i>Fluoroquinolones</i>	0	0.0	14	100.0	1.000	13	92.9	1	7.1	0.472	4	28.6	8	57.1	2	14.3	1.000	0	0.0	7	50.0	7	50.0	0.124	
<i>Gentamicin</i>	0	0.0	98	100.0	1.000	86	87.8	11	11.2	<b>0.026</b>	24	24.5	61	62.2	11	11.2	0.306	0	0.0	73	74.5	25	25.5	0.810	
<i>Linezolid</i>	0	0.0	46	100.0	1.000	43	93.5	3	6.5	<b>0.027</b>	8	17.4	33	71.7	4	8.7	0.067	0	0.0	32	69.6	14	30.4	0.669	
<i>Vancomycin</i>	0	0.0	175	100.0	1.000	146	83.4	27	15.4	<b>0.033</b>	49	28.0	100	57.1	22	12.6	0.870	0	0.0	132	75.4	43	24.6	<b>0.016</b>	
<b>TDM-based therapy adjustment</b>																									
No	0	0.0	1	100.0		1	100.0	0	0.0		1	100.0	0	0.0	0	0.0		1	100.0	0	0.0	0	0.0		
Yes	0	0.0	147	100.0	1.000	128	87.1	19	12.9	<b>0.004</b>	51	34.7	85	57.8	9	6.1	<b>&lt;0.001</b>	0	0.0	147	100.0	0	0.0	-	
Sometimes	0	0.0	54	100.0		35	64.8	17	31.5		5	9.3	29	53.7	17	31.5		0	0.0	0	0.0	54	100.0		
<i>Clinical evidence can outweigh TDM in decisions</i>	0	0.0	33	100.0		25	75.8	7	21.2		4	12.1	20	60.6	8	24.2		0	0.0	0	0.0	33	100.0		
<i>Second TDM sometimes needed</i>	0	0.0	16	100.0	-	11	68.8	4	25.0	-	1	6.3	9	56.3	4	25.0	-	0	0.0	0	0.0	16	100.0	-	
<i>Delayed TDM may be outdated</i>	0	0.0	29	100.0		14	48.3	13	44.8		1	3.4	14	48.3	12	41.4		0	0.0	0	0.0	29	100.0		
<b>Routine TDM for...</b>																									
Yes																									
<i>BTKi</i>	4	5.8	65	94.2		57	82.6	7	10.1		23	33.3	32	46.4	9	13.0		1	1.4	49	71.0	15	21.7		
<i>Bcl-2i</i>	4	4.0	95	96.0		78	78.8	16	16.2		35	35.4	42	42.4	16	16.2		0	0.0	71	71.7	24	24.2		
<i>Bcr-Abl TKi</i>	4	4.3	90	95.7		79	84.0	11	11.7		27	28.7	43	45.7	17	18.1		0	0.0	67	71.3	23	24.5		
<i>FLT3i</i>	3	3.6	81	96.4		64	76.2	16	19.0		28	33.3	37	44.0	13	15.5		0	0.0	60	71.4	21	25.0		
<i>IDH1/2i</i>	3	6.1	46	93.9	-	38	77.6	8	16.3	-	13	26.5	21	42.9	11	22.4	-	0	0.0	36	73.5	10	20.4	-	
No, but would consider																									
<i>If toxicity</i>	0	0.0	59	100.0		42	71.2	16	27.1		12	20.3	41	69.5	5	8.5		0	0.0	41	69.5	18	30.5		
<i>To assure monitoring levels/response</i>	1	1.8	56	98.2		44	77.2	11	19.3		10	17.5	41	71.9	4	7.0		0	0.0	37	64.9	19	33.3		
<i>If suspected interactions</i>	0	0.0	47	100.0		36	76.6	10	21.3		8	17.0	32	68.1	6	12.8		0	0.0	31	66.0	16	34.0		
No, generally not	0	0.0	17	100.0		12	70.6	5	29.4		2	11.8	12	70.6	3	17.6		0	0.0	13	76.5	4	23.5		
<b>Interest related to TDM...</b>																									
Clinical																									
<i>BTKi</i>	4	5.3	71	94.7		54	72.0	17	22.7		23	30.7	36	48.0	11	14.7		0	0.0	52	69.3	19	25.3		
<i>Bcl-2i</i>	4	4.2	91	95.8	-	69	72.6	22	23.2	-	27	28.4	48	50.5	14	14.7	-	0	0.0	67	70.5	24	25.3	-	
<i>Bcr-Abl TKi</i>	4	5.0	76	95.0		60	75.0	16	20.0		21	26.3	38	47.5	15	18.8		0	0.0	51	63.8	25	31.3		
<i>FLT3i</i>	2	2.6	76	97.4		59	75.6	17	21.8		22	28.2	39	50.0	13	16.7		0	0.0	53	67.9	23	29.5		

	TDM availability					TDM performance					TDM turnaround time					TDM-based modification								
	No		Yes		p value	Onsite		Outsourced		p value	<1 day		1-3 days		>3 days		p value	No		Yes		At times		p value
	n	%	n	%		n	%	n	%		n	%	n	%	n	%		n	%	n	%	n	%	
<i>IDH1/2i</i>	2	4.1	47	95.9		36	73.5	11	22.4		11	22.4	24	49.0	10	20.4		0	0.0	31	63.3	16	32.7	
Research																								
<i>BTKi</i>	1	1.9	52	98.1		42	79.2	10	18.9		14	26.4	27	50.9	10	18.9		0	0.0	34	64.2	18	34.0	
<i>Bcl-2i</i>	1	1.4	68	98.6		53	76.8	15	21.7		21	30.4	34	49.3	12	17.4		0	0.0	48	69.6	20	29.0	
<i>Bcr-Abl TKi</i>	2	4.1	47	95.9		36	73.5	11	22.4		12	24.5	25	51.0	10	20.4		0	0.0	31	63.3	16	32.7	
<i>FLT3i</i>	2	3.2	60	96.8		45	72.6	15	24.2		19	30.6	33	53.2	8	12.9		0	0.0	43	69.4	17	27.4	
<i>IDH1/2i</i>	1	2.4	41	97.6		29	69.0	12	28.6		9	21.4	25	59.5	7	16.7		0	0.0	28	66.7	13	31.0	

Bcl-2i, B-cell lymphoma 2 inhibitor; Bcr-Abl TKi, breakpoint cluster region–Abelson tyrosine kinase inhibitor; BTKi, Bruton tyrosine kinase inhibitor; CAR-T, chimeric antigen receptor t-cell therapy; FLT3i, FMS-like tyrosine kinase 3 inhibitor; HSCT, hematopoietic stem cell transplantation; IDH1/2i, isocitrate dehydrogenase 1/2 inhibitor; p value, probability value (statistical significance); TDM, therapeutic drug monitoring.