

Table S1. Characteristic orbiSIMS peaks of 20 mL olaparib at 1 mg/ml with 20 mg homogenised rat brain tissue (final drug concentration= 0.5% [w/w]).

No.	Center Mass (u) Assignment Description			Brain control		Olaparib + Brain	
				Area	Mass deviation (ppm)	Area	Mass deviation (ppm)
1	253.0783	C ₁₅ H ₁₀ FN ₂ O ⁻	Fragment	0	+12.3	344242	+0.4
2	433.1677	C ₂₄ H ₂₂ FN ₄ O ₃ ⁻	Molecular ion	0	-8.2	1475956	-1.1
3	145.0406	C ₈ H ₅ N ₂ O ⁻	Fragment	93	-4.2	14100	-1.2
4	159.0561	C ₉ H ₇ N ₂ O ⁻	Fragment	0	+5.3	2111	-1.5
5	181.0982	C ₉ H ₁₃ N ₂ O ₂ ⁻	Fragment	0	-4.2	9125	-0.5
6	153.1032	C ₈ H ₁₃ N ₂ O ⁻	Fragment	0	-4.6	7751	-1.1
7	365.1415	C ₂₀ H ₁₈ FN ₄ O ₂ ⁻	Fragment	0	+1.3	11365	-1.1
8	255.2329	C ₁₆ H ₃₁ O ₂ ⁻	Brain lipid	38992508	+1.7	47806478	+0.4
9	152.9957	C ₃ H ₆ PO ₅ ⁻	Brain lipid	4075584	+0.3	2167331	-1.1
10	281.2486	C ₁₈ H ₃₃ O ₂ ⁻	Brain lipid	84148602	+1.3	86463483	-0.0
11	385.3473	C ₂₇ H ₄₅ O ⁻	Brain cholesterol	542562	+0.4	560758	-0.8

Table S2. Characteristic orbiSIMS peaks of 20 mL etoposide at 1 mg/ml with 20 mg homogenised rat brain tissue (final drug concentration = 0.5% [w/w]).

No.	Center Mass (u) Assignment Description			Brain control		Etoposide + Brain	
				Area	Mass Deviation (ppm)	Area	Mass Deviation (ppm)
1	587.176476	C ₂₉ H ₃₁ O ₁₃ ⁻	Molecular ion	0	+10.1	195128	-0.0
2	435.129253	C ₂₁ H ₂₃ O ₁₀ ⁻	Fragment	0	+4.5	257	+0.3
3	153.055473	C ₈ H ₉ O ₃ ⁻	Fragment	0	-2.0	126371	-1.6
4	383.113165	C ₂₁ H ₁₉ O ₇ ⁻	Fragment	0	-5.7	168101	+0.2
5	255.2329	C ₁₆ H ₃₁ O ₂ ⁻	Brain lipid	38992508	+1.7	42640092	+1.4
6	152.9957	C ₃ H ₆ PO ₅ ⁻	Brain lipid	4075584	+0.3	4080847	-0.0
7	281.2486	C ₁₈ H ₃₃ O ₂ ⁻	Brain lipid	84148602	+1.3	84980993	+1.1
8	385.3473	C ₂₇ H ₄₅ O ⁻	Brain cholesterol	542562	+0.4	420006	+0.1

Table S3. Characteristic orbiSIMS peaks of 20 mg/mL olaparib in homogenised rat brain tissue

No.	Center Mass (u)	Assignment	Description	Brain control		Olaparib + Brain	
				Area	Mass deviation (ppm)	Area	Mass deviation (ppm)
1	253.0783	C ₁₅ H ₁₀ FN ₂ O ⁻	Fragment	0	+12.3	8130	
2	433.1677	C ₂₄ H ₂₂ FN ₄ O ₃ ⁻	Molecular ion	0	-8.2	68148	
3	145.0406	C ₈ H ₅ N ₂ O ⁻	Fragment	93	-4.2	91220	
4	159.0561	C ₉ H ₇ N ₂ O ⁻	Fragment	0	+5.3	35794	
5	181.0982	C ₉ H ₁₃ N ₂ O ₂ ⁻	Fragment	0	-4.2	259033	
6	153.1032	C ₈ H ₁₃ N ₂ O ⁻	Fragment	0	-4.6	154525	
7	365.1415	C ₂₀ H ₁₈ FN ₄ O ₂ ⁻	Fragment	0	+1.3	95	
8	255.2329	C ₁₆ H ₃₁ O ₂ ⁻	Brain lipid	38992508	+1.7	34119796	
9	281.2486	C ₁₈ H ₃₃ O ₂ ⁻	Brain lipid	84148602	+1.3	52791661	
10	385.3473	C ₂₇ H ₄₅ O ⁻	Brain cholesterol	542562	+0.4	4664140	

Table S4. Characteristic orbiSIMS peaks of 20 mL vorinostat at 1 mg/ml with 20 mg homogenised rat brain tissue (final drug concentration = 0.5% [w/w]).

No.	Center Mass (u)	Assignment	Description	Brain control		Vorinostat + brain	
				Area	Mass deviation (ppm)	Area	Mass deviation (ppm)
1	263.1397	C ₁₄ H ₁₉ N ₂ O ₃ ⁻	M-H	353	-1.5	1687335	-0.6
2	264.1431	C ₁₄ H ₂₀ N ₂ O ₃ ⁻	M	0	-16.4	166727	-1.4
3	202.1244	C ₁₃ H ₁₆ NO ⁻	Fragment	311	3.1	70003	-1.1
4	176.1083	C ₁₁ H ₁₄ NO ⁻	Fragment	176	1.4	1145	-1.9
5	190.1228	C ₁₂ H ₁₆ NO ⁻	Fragment	0	-4.7	563	-0.9
6	204.1394	C ₁₃ H ₁₈ NO ⁻	Fragment	306	0.1	4835	-1.1
7	247.1452	C ₁₄ H ₁₉ N ₂ O ₂ ⁻	Fragment	848	-0.1	10259	-0.8
8	172.0978	C ₈ H ₁₄ NO ₃ ⁻	Fragment	494	2.7	1229	1.2
9	187.1096	C ₈ H ₁₅ N ₂ O ₃ ⁻	Fragment	0	4.1	2209	-1.1
10	255.2339	C ₁₆ H ₃₁ O ₂ ⁻	Brain lipid	24792697	1.2	24431231	0.0
11	281.2486	C ₁₈ H ₃₃ O ₂ ⁻	Brain lipid	42916135	0.9	38923936	-0.4
12	385.3473	C ₂₇ H ₄₅ O ⁻	Brain cholesterol	3582325	-0.3	43333052	-1.5

Table S5. Characteristic orbiSIMS peaks of 20 mL gemcitabine at 1 mg/ml with 20 mg homogenised rat brain tissue (final drug concentration = 0.5% [w/w]).

No.	Center Mass (u)	Assignment	Description	Brain control		Gemcitabine + brain	
				Area	Mass deviation (ppm)	Area	Mass deviation (ppm)
1	262.0650	C ₉ H ₁₀ F ₂ N ₃ O ₄ ⁻	Molecular ion	0	2	101904	1.2
2	247.0539	C ₉ H ₉ F ₂ N ₂ O ₄ ⁻	Fragment	0	3.5	419	0.4
3	246.0704	C ₉ H ₁₀ F ₂ N ₃ O ₃ ⁻	Fragment	0	3.4	658	-0.3
4	232.0544	C ₈ H ₈ F ₂ N ₃ O ₃ ⁻	Fragment	0	1.9	1189	-1.6
5	244.0731	C ₉ H ₁₁ FN ₃ O ₄ ⁻	Fragment	387	-3.2	1892	-0.3
6	243.0657	C ₉ H ₁₀ FN ₃ O ₄ ⁻	Fragment	0	0.7	774	0.0
9	255.2339	C ₁₆ H ₃₁ O ₂ ⁻	Brain lipid	24792697	1.2	140961907	2.1
10	281.2486	C ₁₈ H ₃₃ O ₂ ⁻	Brain lipid	42916135	0.9	277414449	1.8
11	385.3473	C ₂₇ H ₄₅ O ⁻	Brain cholesterol	3582325	-0.3	35431934	0.5

Table S6. Characteristic orbiSIMS peaks of 20 mL dasatinib at 1 mg/ml with 20 mg homogenised rat brain tissue (final drug concentration = 0.5% [w/w]).

No.	Center Mass (u)	Assignment	Description	Brain control		Dasatinib + brain	
				Area	Mass deviation (ppm)	Area	Mass deviation (ppm)
1	261.1457	C ₁₂ H ₁₇ N ₆ O ⁻	Fragment	0	-4.8	7466588	0.6
2	231.1375	C ₁₁ H ₁₅ N ₆ ⁻	Fragment	396	7.1	690695	1.8
3	217.1194	C ₁₀ H ₁₃ N ₆ ⁻	Fragment	0	-6.0	938722	-0.8
4	174.0786	C ₈ H ₈ N ₅ ⁻	Fragment	1151	3.6	1676612	1.0
5	172.0628	C ₈ H ₆ N ₅ ⁻	Fragment	3692	2.9	1131926	-0.6
6	160.0627	C ₇ H ₆ N ₅ ⁻	Fragment	17561	2.7	7009838	-0.5
7	319.1326	C ₁₄ H ₁₉ N ₆ OS ⁻	Fragment	0	-4.6	4466339	1.1
8	486.1449	C ₂₂ H ₂₅ C ₁₂ N ₇ O ₂ S ⁻	M-H	0	-6.2	4444771	1.0
9	255.2339	C ₁₆ H ₃₁ O ₂ ⁻	Brain lipid	24792697	1.2	4787061	0.5
10	281.2486	C ₁₈ H ₃₃ O ₂ ⁻	Brain lipid	42916135	0.9	7523922	0.3
11	385.3473	C ₂₇ H ₄₅ O ⁻	Brain cholesterol	3582325	-0.3	2268736	-0.8