

Table S1. Clinical information. MM cohort's characteristics are listed.

Induction therapy	Patients n=(%)
Non-antiCD38-based	23 (52)
AntiCD38-based	21 (48)
Induction response	
≥VGPR	24 (60)
<VGPR	16 (40)
Transplant (TX)	
Yes	40 (91)
No	4 (9)
TX response	
≥VGPR	21 (54)
<VGPR	18 (46)

VGPR=very good partial response; TX=transplant

Table S2. CMMCs count, single cell separation, and genomic analysis quality results.

Samples	CMMCs count	CMMCs redetected in DEPArray (%)	CMMCs recovered (%)	CMMCs passing Ampli1 WGA QC (%)	CMMCs passing Ampli1 LowPass QC (%)	CMMCs with interpretable CNA profiles (%)	CMMCs Aberrant (%)
CMMC01	15	5 (33%)	5 (100%)	3 (60%)	3 (100%)	3 (100%)	3 (100%)
CMMC02	16	7 (44%)	2 (29%)	2 (100%)	2 (100%)	2 (100%)	2 (100%)
CMMC03	32	13 (41%)	10 (77%)	8 (89%)	6 (75%)	6 (100%)	6 (100%)
CMMC04	62	42 (68%)	23 (55%)	21 (95%)	21 (100%)	21 (100%)	19 (90%)
TOTAL	125	67 (54%)	40 (60%)	34 (85%)	32 (94%)	32 (100%)	30 (94%)

WGA=whole genome amplification; QC=quality control; CNA=copy number alteration

Table S3. Biochemical parameters at different timepoint for each patient, with the relative CMMCs count.

Patient ID	Pathology	Time-point (m)	CMMCs count	Total protein (g/dL)	M-protein (%)	M-protein (g/dL)	LDH (IU/L)	Creatinine (mg/dL)	β2G (%)	B2G (g/dL)	K/L ratio	Calcium (mg/dL)	CRP (mg/dL)	Albumin (%)	Albumin (g/dL)	WBC (x10 ⁹ /L)	Hemoglobin (g/dL)	Hematocrit (%)	Platelets (x10 ⁹ /L)	β2M (mg/L)
AIRC19_001	SMM	17	22	8.4	31.5	2.65	117.1	1.02	40.2	3.38	0.04	9.40	0.04	40.7	3.42	3.65	13.60	39.90	260	3.60
AIRC19_001	SMM	21	2	8.7	31.6	2.75	120.6	1.15	40.6	3.53	0.03	9.27	0.19	39.8	3.46	4.01	13.60	42.20	267	4.79
AIRC19_001	SMM	38	52	8.6	32.7	2.81	124.9	1.10	40.9	3.52	0.04	9.35	0.04	40.8	3.51	4.52	14.40	44.60	259	3.47
AIRC19_004	MM	0					160	1.15			24.40	9.9	0.1		4.40		10.40		234	3.4
AIRC19_004	MM	9	0																	
AIRC19_004	MM	12	2	6.42	4.5	0.29	171.3	1.08	3.6	0.23	3.48	9.14	0.23	64.1	4.12	3.56	9.60	27.70	144	
AIRC19_012	MM	0					163	0.65				9.3	0.27				11.60		237	
AIRC19_012	MM	18	0													4.65	11.70	35.90	215	
AIRC19_013	MM	0	0	5.9	4.3	0.25	187.3	0.58	4.9	0.29	10.79	8.70	0.28	57.2	3.37	3.06	12.20	35.00		2.74
AIRC19_013	SMM	12	24	7.2	16.2	1.17	162.5	0.60	4.7	0.34	65.42	8.80	0.23	50.0	3.60	4.84	11.80	36.60	298	
AIRC19_013	SMM	23	100	7.0	14.9	1.04	157.0	0.60	4.5	0.32	67.19	8.83	0.20	50.9	3.56	5.62	12.40	38.00	303	2.51

AIRC19_013	MM	30	4	7.1	17.9	1.27	161.6	0.67	4.5	0.32	105.86	8.72	0.20	50.3	3.57	4.79	12.30	37.50	247	2.50
AIRC19_014	MM	0	371				156	0.87				9.50	0.46						436.0	1.90
AIRC19_014	MM	7	1	6.6	10.6	0.70	140.9	0.67	3.1	0.20		9.60	0.38	64.4	4.24	22.59	12.00	34.00		1.80
AIRC19_014	MM	12	8	7.4	10.3	0.76	146.8	0.86	3.0	0.22	2.85	10.04	0.07	63.2	4.68	4.94	12.80	37.10	202.0	1.81
AIRC19_016	MM	0				2.00	137	1.97			16.00	11.5	1.38		3.28		13.50		264	6.1
AIRC19_016	MM	5	0																	
AIRC19_016	MM	10	1	5.2	x	x	139	1.86	4.3	0.22	1.41	8.7	2.85	67.8	3.53	3.16	8.30	22.10	16	3.49
AIRC19_018	MM	0					243	0.89				11.4	0.07		4.12		9.00		435	5.7
AIRC19_018	MM	4	0																	
AIRC19_018	MM	7	0	6.39	1.1	0.07	139.3	1.23	3.2	0.20	2.83	9.5	0.07	71.5	4.57	33.26	8.80	25.30	67	
AIRC19_019	MM	0					167	0.75				9.2	0.23		4.30		14.80		232	
AIRC19_019	MM	3	0																	
AIRC19_019	MM	6	3	6.8	1.3	0.09	227	0.87	4.6	0.31	3.05	10	0.25	66.8	4.54	4.49	13.60	41.30	237	
AIRC19_019	MM	8	12	6.6	1.3	0.09	263	0.67	4.5	0.30	3.17	9.5	2.6	66.3	4.38	8.98	11.20	31.90	38	
AIRC19_020	MM	0					234	0.64			489.00	9.3	0.24		4.00		12.00		174	1.6
AIRC19_020	MM	3	62																	
AIRC19_020	MM	8	0	5.2	x	x	199	0.68	5.4	0.28	0.94	8.7	0.8	59.7	3.10	0.14	10.10	27.60	42	2
AIRC19_021	SMM	2	52																	
AIRC19_021	SMM	7	159	10.0	31.3	3.13	162.4	0.81	40.2	4.02	0.03	11.30	0.67	43.1	4.31	5.85	12.20	39.00	316	1.91
AIRC19_021	SMM	13	49	9.2	37.3	3.43	160.0	0.85	41.7	3.84	0.03	11.04	0.55	43.0	3.96	5.38	11.60	37.00	247	2.26
AIRC19_021	SMM	26	138	10.5	35.7	3.75	160.1	0.75	42.4	4.45	0.03	11.93	0.46	41.0	4.31	5.84	12.40	39.90	241	1.99
AIRC19_023	MM	0	55				155	5.39				10.07							586.0	5.00
AIRC19_024	MM	0		12.0		49.00	150	0.67	50.0	6.00		9.70	0.21	34.0	4.08		12.60		262.0	2.60
AIRC19_024	MM	1	16	5.6	x	x	194.5	0.78	3.8	0.21	0.00	9.12	0.84	62.3	3.49	4.95	11.70	34.40	236	
AIRC19_024	MM	5	1	5.8	0.9	0.05	179.9	0.59	4.5	0.26	0.01	9.12	0.22	65.7	3.81	3.69	12.50	36.00	200	
AIRC19_024	MM	5	0	4.96	x	x	104.1	0.66	5	0.25		8.08	3.47	61.5	3.05	0.22	11.10	31.60	69	
AIRC19_024	MM	12	0	5.75	x	x	183.7	0.74	4.1	0.24	0.90	9.57	0.17	66.1	3.80	2.33	12.20	35.30	140	
AIRC19_026	MM	0	133				140	0.71		0.00		9.10	3.50		0.00				222.0	3.29
AIRC19_026	MM	3	5	6.6	6.7	0.44	206.9	0.75	4.5	0.30	2.04	8.89	0.67	57.0	3.76	4.03	11.60	33.90	314.0	
AIRC19_026	MM	11	5	6.0	x	x	263.8	0.56	5.0	0.30	1.00	9.03			0.00	5.45	10.60	33.20	292.0	3.83
AIRC19_027	MM	0	18588				171	1.52		0.00		8.00	3.22		0.00				154.0	49.70
AIRC19_027	MM	3	15	6.1	x	x	227.1	0.99		0.00		9.15			0.00	2.34	11.90	35.20	233.0	
AIRC19_027	MM	11	0	5.7	6.7	0.38	192.9	0.93	3.3	0.19	3.13	9.27	0.11	63.8	3.64	3.16	12.40	36.20	99.0	3.91
AIRC19_027	MM	18	3	5.5	6.0	0.33	208.9	1.01	4.2	0.23	0.74	9.14	1.23	67.3	3.67	4.59	11.70	33.70	120.0	
AIRC19_028	MM	0		8.4	27.4	2.30	143	0.96	2.2	0.18	4.38	9.10	0.03	49.4	4.15	8.67	10.60	33.70	202.0	3.90
AIRC19_028	MM	1	54	9.6	32.8	3.15	135	1.01	1.8	0.17	7.73	9.3	0.04	47.4	4.55	7.13	10.60	31.20	142	3.8
AIRC19_028	MM	17	2	6.5	2.9	0.19	161	0.84	3.5	0.23		9.5	0.02	69.2	4.50	5.45	11.70	33.80	143	1.5
AIRC19_029	MM	0	1	8.2	18.8	1.54	184.9	0.71	2.6	0.21	319.50	10.23	0.03	57.6	4.71	5.68	12.50	37.50	326.0	1.52
AIRC19_029	MM	8	0	6.5	6.8	0.44	228.4	0.67	4.1	0.27	21.53	9.78	0.02	63.6	4.13	10.42	11.20	33.80	382.0	1.40
AIRC19_030	MM	1	316	7.4	9.9	0.73	183.8	0.6	4.0	0.30	0.01	9.42	0.11	60.8	4.50	6.55	11.90	36.90	344.0	1.20
AIRC19_030	MM	6	0	6.0	x		133	0.55	3.7	0.22	0.63	8.86	0.13	67.6	4.06	5.18	12.40	38.10	279.0	1.38
AIRC19_030	MM	10	6	6.0	1.0	0.06	160.7	0.58	3.7	0.22	0.80	9.38	0.08	68.2	4.09	4.09	11.30	37.80	255.0	1.71
AIRC19_030	MM	13	0	5.8	1.1	0.06	166.8	0.56	3.6	0.21	0.58	9.07	0.12	69.4	4.03	2.85	11.10	33.50	219.0	
AIRC19_031	MM	0	15	7.4	18.8	1.39	424	0.76	2.9	0.21	7.03	9.3	0.22	49.3	3.65	5.01	10.50	29.80	227	
AIRC19_031	MM	0		10.8	32.3	3.49	814	0.89	1.9	0.21	41.53	9.90	0.09	40.6	4.38	5.85	10.90	32.60	186.0	4.40
AIRC19_031	MM	6	0	7.1	6.8	0.48	299	0.72	3.3	0.23	2.05	10	0.12	61.6	4.37	5.60	11.20	33.20	181	2.9

AIRC19_031	MM	10	0	6.4	2.9	0.19	195	0.79	3.6	0.23	2.00	9.7	0.06	64.7	4.14	5.93	11.40	33.30	170	
AIRC19_033	MM	0		8	21.9	1.75	275	0.73	3.4	0.27	142.07	9	0.78	49.7	3.98	4.51	18.80	37.70	206	2.01
AIRC19_033	MM	1	65	8.3	24.1	2.00	226	0.73	3.5	0.29	97.43	8.9	0.34	50	4.15	5.46	12.60	37.30	220	2.1
AIRC19_033	MM	6	897	6.5	1.7	0.11	178	0.62	5.4	0.35	1.34	9.2	0.33	58.7	3.82	3.74	10.20	32.60	188	
AIRC19_033	MM	11	0	6.7	x	x	209	0.88	3.8	0.25	1.34	9.3	0.36	61.8	4.14	4.35	10.90	34.40	227	
AIRC19_035	MM	0	39940	9.0	48.4	4.36	109.4	0.93	2.6	0.23	47.18	7.57	4.45	23.8	2.14	7.18	8.90	26.30	146.0	8.37
AIRC19_035	MM	6	0	6.7	5.7	0.38	150	0.86	3.3	0.22	15.22	9.03	0.59	62.8	4.21	6.06	13.60	38.00	116.0	3.21
AIRC19_036	MM	0	736	6.8	1.3	0.09	173	1.43	12.6	0.86	0.03	10.04	0.05	66.0	4.49	5.45	11.00	32.70	175.0	4.18
AIRC19_036	MM	4	0	6.4	1.5	0.10	179.8	0.68	3.6	0.23	0.70	9.58	0.10	70.4	4.51	5.79	15.00	44.80	171.0	
AIRC19_036	MM	15	0	6.2	1.5	0.09	189	0.73	4.4	0.27	1.51	9.80	0.20	69.3	4.30	6.11	14.10	41.70	222.0	
AIRC19_037	MM	0	576	10.6	36.7	3.89	155.3	0.88	55.0	5.83	197.52	8.68	0.07	32.4	3.43	2.16	10.10	30.50	181.0	4.41
AIRC19_037	MM	4	18	8.1	34.2	2.78	195.3	1.04	43.6	3.55	191.55	8.67	0.14	40.5	3.30	2.27	11.10	34.20	178.0	
AIRC19_037	MM	8	0	6.1	8.3	0.51	307	1.1	17.6	1.07	21.27	8.74	0.31	59.1	3.61	2.79	10.00	28.90	223.0	3.00
AIRC19_037	MM	14	1	6.0	1.2	0.07	281.3	1	3.6	0.22	1.41	9.95	0.19	71.8	4.31	3.54	12.00	35.80	164.0	4.72
AIRC19_038	MM	0	2335	9.1	24.1	2.19	175.5	0.57	3.7	0.34	1.82	9.27	3.62	38.3	3.49	6.12	12.10	37.80	294.0	2.97
AIRC19_038	MM	7	0	6.2	x	x	253.9	0.68	4.5	0.28	1.93	9.67	0.90	68.3	4.23	5.12	11.70	35.20	170.0	2.16
AIRC19_038	MM	17	0	5.8	x	x	258.3	0.51	5.3	0.31	0.82	7.59	9.29	56.6	3.28	4.57	10.20	31.20	141.0	
AIRC19_039	MM	0		9.7	41.8	4.05	109	1.19	50.5	4.90	0.02	9.10	0.18	31.9	3.09	3.41	9.70	29.10	129.0	3.86
AIRC19_039	MM	1	9	7.6	2.5	0.19	145	0.81	29.8	2.26	0.12	9	0.22	46.8	3.56	4.36	12.60	39.20	295	
AIRC19_039	MM	2	0	6	4.5	0.27	203	0.71	12.3	0.74	0.71	8.9	0.28	61.3	3.68	4.16	13.70	41.20	346	
AIRC19_039	MM	6	5	6.4	3.9	0.25	216	0.93	9.9	0.63	1.01	9.1	0.47	59.8	3.83	5.26	15.90	46.70	236	
AIRC19_039	MM	12	2	6.9	2.3	0.16	202	0.99	8	0.55	0.75	9.8	0.33	62.4	4.31	5.82	17.30	48.80	185	
AIRC19_040	MM	0	1491	5.5	0.5	0.03	355.5	0.7	5.1	0.28	514.73	8.56	0.75	54.7	3.01	7.29	8.50	26.20	213.0	10.27
AIRC19_051	MM	0	960	7.0	14.3	1.00	192.1	0.78	3.2	0.22	67.29	8.97	0.15	57.9	4.05	3.98	14.00	42.60		2.47
AIRC19_051	SMM	1	976	6.7	15.9	1.07	188.2	0.81	3.3	0.22	29.42	9.09	0.16	57.1	3.83	5.16	13.80	42.60	280	2.26
AIRC19_053	MM	0		7.9	10.9	0.86	205.6	0.56	19.2	1.52	1.86	9.86	0.15	51.0	4.03	4.55	11.50	34.60	444	1.97
AIRC19_053	MM	1	27	6.4	2.8	0.18	225	0.6	8.4	0.54	1.24	8.9	1.17	55.4	3.55	5.29	11.90	35.90	251	
AIRC19_053	MM	5	21	5.9	x	x	326	0.58	4.2	0.25	0.94	9.3	0.43	62.1	3.66	45.08	11.70	35.60	243	
AIRC19_053	MM	15	79	6.2	x	x	278	0.51	4.5	0.28	0.94	7.8	0.26	57.3	3.55	5.23	10.80	32.80	354	1.7
AIRC19_054	MM	0	38	10.0	36.0	3.60	107.0	0.92	52.1	5.21	0.03	9.03	0.17	34.7	3.47	4.48	13.10	38.00		3.04
AIRC19_054	SMM	1	327	9.7	35.8	3.47	94.2	0.95	50.0	4.85	0.03	9.39	0.06	36.6	3.55	5.02	13.90	40.60	159	
AIRC19_054	MM	4	10	6.5	1.4	0.09	180.6	0.73	7.1	0.46	1.17	9.30	0.04	65.2	4.24	6.31	13.80	40.60		
AIRC19_054	MM	9	28	7.2	2.9	0.21	182.4	1.01	9.2	0.66	1.01	9.78	0.07	62.1	4.47	8.16	15.40	44.60	167	1.68
AIRC19_054	MM	13	19	7.7	2.6	0.20	178.0	0.74	3.8	0.29	1.72	9.43	0.06	60.6	4.67	6.12	13.10	37.80	131	2.51
AIRC19_055	MM	3	0	5.5	1.0	0.06	199.8	1.09	4.7	0.26	0.55	8.52	5.19	56.0	3.08	6.72	10.40	31.70	258	
AIRC19_055	SMM	4	2463	7.8	15.0	1.17	161.0	0.99	3.1	0.24	0.08	9.26	0.34	52.6	4.10	6.29	10.60	34.20	159	3.33
AIRC19_055	MM	7	0	5.8			211.2	1.06	4.4	0.26	0.93	8.93	1.63	58.6	3.40	5.42	11.20	34.70	224	3.59
AIRC19_055	SMM	11	390	8.0	14.3	1.14	161.0	1.19	3.5	0.28	0.06	9.10	0.55	48.5	3.88	4.93	9.90	32.40	143	
AIRC19_055	MM	16	619	7.6	16.3	1.24	185.5	1.35	3.8	0.29	0.07	9.79	0.48	48.2	3.66	5.76	9.60	29.00	188	3.91
AIRC19_056	MM	0		6.9	x	x	165.4	0.56	5.2	0.36	389.02	9.45	0.06	60.9	4.19	7.22	13.90	39.70	322	2.31
AIRC19_056	MM	4	1	6.58	x	x	168.8	0.52	3.6	0.24	2.15	9.52	0.03	64.3	4.23	6.08	14.90	43.50	408	1.73
AIRC19_057	MM	0	13	9.1	19.1	1.75	186.7	0.77	3.1	0.28	19.58	9.39	0.19	44.4	4.06	5.07	12.50	37.00	312.0	2.08
AIRC19_057	MM	5	0	8.2	16.9	1.39	179.9	0.79	3.2	0.26	12.24	9.14	0.10	51.7	4.24	6.44	13.00	38.20	282.0	
AIRC19_057	MM	9	0	6.2	4.9	0.30	241.6	0.84	4.1	0.25	2.46	8.31	0.36	61.2	3.79	6.40	9.60	29.00	408.0	1.70
AIRC19_057	MM	15	12	7.2	3.1	0.22	193.1	0.99	4.2	0.30	2.35	9.24	0.35	60.4	4.35	5.17	10.90	32.40	255.0	2.14
AIRC19_058	MM	0		10.7	36.0	3.85	143	0.87	3.5	0.37	75.33	10.00	1.52	35.1	3.76	7.25	13.00	38.50	354.0	3.50

AIRC19_058	MM	1	0	8.4	28.6	2.40	191	0.79	3.9	0.33	30.02	8.5	2.27	38.6	3.24	4.93	12.40	38.30	558	
AIRC19_058	MM	6	4	6.5	8.2	0.53	190	0.76	4.2	0.27	6.96	8.4	0.68	54.9	3.57	6.34	13.80	39.70	280	
AIRC19_058	MM	11	43	6.4	8.4	0.54	214	0.79	4.3	0.28	5.96	9	0.42	58.8	3.76	5.30	14.00	39.70	249	1.8
AIRC19_058	MM	15	7																	
AIRC19_058	MM	19	180	8.5	28.4	2.41	155	0.77	3.7	0.31	643.25	9.1	8.66	38	3.23	8.16	11.00	32.50	362	21.8
AIRC19_059	MM	0		11	32.5	3.58	185	0.93	2.2	0.24	40.93	8.9	0.28	38.9	4.28	5.29	8.80	26.90	190	5.15
AIRC19_059	MM	2	220	10.2	33.2	3.39	200	1.1	2.6	0.27	71.19	8	0.86	39.3	4.01	3.84	8.90	27.30	208	
AIRC19_059	MM	10	0	6.3	2.1	0.13	160	0.95	4	0.25	1.70	9	0.22	65.4	4.12	6.20	13.50	41.70	170	
AIRC19_059	MM	14	0	5.9	0.8	0.05	150	1.12	4.1	0.24	2.27	9.2	0.14	67.3	3.97	4.51	13.40	39.50	224	
AIRC19_059	MM	19	0	5.9	1.1	0.06	167	0.96	3.8	0.22	2.41	9.2	0.12	66.7	3.94	5.75	14.20	40.80	264	
AIRC19_060	MM	0	11	8.3	17.0	1.41	184	0.75	29.2	2.42	25.24	9.66	0.17	47.4	3.94	3.16	12.90	37.70	139.0	1.33
AIRC19_060	MM	4	2	6.2	x	x	271.5	0.71	3.3	0.20	1.67	9.36	0.36	67.3	4.17	4.92	13.20	41.10	194.0	
AIRC19_060	MM	9	1	6.5	x	x	283.2	0.8	3.2	0.21	1.07	9.48	0.16	69.5	4.52	2.75	14.30	40.70	161.0	1.40
AIRC19_060	MM	13	0	6.2	x	x	283.6	0.91	2.6	0.16	1.69	9.15	0.21	71.0	4.40	3.14	12.10	33.90	110.0	1.45
AIRC19_071	MM	0		6.7	1.6	0.11	196.9	0.81	6.3	0.42	2.90	9.59	0.42	60.1	4.03	7.96	15.00	44.60	228.0	1.16
AIRC19_071	MM	1	0	6.52	x	x	162.1	0.85	6.7	0.44	1.29	9.6	0.95	60.5	3.94	5.13	15.10	44.60	319	
AIRC19_072	MM	0		8.9	29.9	2.66	101	0.79	38.8	3.45	17.50	10.11	0.13	39.2	3.49	4.22	11.30	34.20	220	3.1
AIRC19_072	MM	1	1	7.9	21	1.66	120	0.87	31	2.45	9.86	9.5	0.79	42.8	3.38	2.82	11.50	35.10	368	
AIRC19_072	MM	5	12	7.6	21.2	1.61	121	0.73	36.7	2.79	16.53	8.9	0.28	41	3.12	3.75	11.60	34.90	351	
AIRC19_074	MM	0	0	8.4	24.8	2.08	140	0.94	2.8	0.24	0.15	9.8	0.19	46.2	3.88	3.88	13.30	37.30	207	2.8
AIRC19_074	MM	0		8.01	22.8	1.83	143.2	1.01	2.6	0.21	0.16	9.56	0.24	46.8	3.75	4.08	12.40	35.90	243	2.78
AIRC19_074	MM	5	0	6.5	2	0.13	176	0.93	4.4	0.29	1.18	9.6	0.13	71.1	4.62	3.79	13.40	36.50	170	
AIRC19_074	MM	11	0	6	x	x	251	0.73	4.9	0.29	7.95	9.5	0.16	67.2	4.03	4.38	11.80	33.30	197	
AIRC19_075	SMM	8	344	6.5	x	x	196.1	0.78	4.5	0.29	96.69	10.13	0.30	67.5	4.39	4.69	14.80	42.60	163	1.57
AIRC19_075	SMM	12	656	6.3	x	x	209.7	0.93	4.0	0.25	97.68	9.69	0.16	71.2	4.49	4.84	15.60	46.10	145	1.72
AIRC19_075	SMM	16	371	6.2	x	x	215.3	0.90	4.0	0.25	125.25	9.52	0.17	70.2	4.35	4.99	15.30	45.70	131	
AIRC19_081	MM	0		7.0	1.3	0.09	320.4	1.31	4.5	0.32	32.35	9.78	1.01	59.6	4.17	4.40	9.00	26.70	201	8.39
AIRC19_081	MM	3	0	5.54	x	x	128.9	0.8	4	0.22	1.27	8.82	0.59	68.5	3.79	2.64	11.10	34.30	218	
AIRC19_081	MM	9	0	5.94	x	x	184.6	0.99	4.4	0.26	0.85	9.07	0.2	66.6	3.96	5.17	11.80	35.40	307	
AIRC19_082	MM	0		8.64	25.2	2.18	218.3	0.58	4.2	0.36	14.34	9.2	0.31	42.9	3.71	5.18	12.30	37.70	208	3.01
AIRC19_082	MM	2	0	5.7	2.8	0.16	161	0.82	3.9	0.22	1.55	9.1	0.20	66.3	3.78	4.93	11.80	36.10	298	
AIRC19_082	MM	10	0	6.8	x	x	216	0.88	4.1	0.28	1.83	8.9	0.11	35.3	2.40	4.11	12.40	38.10	84	1.7
AIRC19_083	MM	0		9.7	32.3	3.13	164	0.66	2.2	0.21	41.79	8.9	0.06	39.1	3.79	3.64	11.20	31.90	279	2.6
AIRC19_083	MM	4	0	6	4.2	0.25	194	0.68	4	0.24	2.74	9.5	0.09	64.1	3.85	3.24	12.50	36.40	214	
AIRC19_083	MM	11	0	5.8	3.1	0.18	194	0.69	3.3	0.19	2.32	8.6	0.05	69.1	4.01	2.54	10.80	32.10	117	
AIRC19_084	MM	0		11.6	52.1	6.04	85.5	0.74	61.2	7.10	257.20	10.37	0.03	28.1	3.26	6.10	9.40	28.60	130	3.19
AIRC19_084	MM	2	5432	10.82	43.2	4.67	95	0.71	1.9	0.21	317.92	10.14	0.11	30.4	3.29	2.70	11.50	35.30	232	
AIRC19_085	MM	0		9.48	38.9	3.69	121	0.9	2	0.19	0.02	9.34	0.27	41.5	3.93	5.26	11.60	33.40	237	4
AIRC19_085	MM	5	333	6.1	6.5	0.40	155	0.77	3	0.18	0.33	9.4	0.13	68.3	4.17	4.11	12.40	36.70	279	
AIRC19_085	MM	10	68	6.4	7.9	0.51	153	0.87	3.2	0.20	0.16	9.3	0.16	65.7	4.20	3.68	12.70	37.30	195	2.19
AIRC19_088	MM	0		9.3	37.2	3.46	132.6	1.14	2.8	0.26	0.06	8.92	0.22	40.4	3.76	6.41	13.70	38.00	246	2.4
AIRC19_088	MM	3	178	7.9	24.6	1.94	152	0.91	3.6	0.28	0.16	8.9	0.44	48.9	3.86	6.18	13.10	38.10	280	
AIRC19_088	MM	8	74	7.6	17.5	1.33	154	0.97	3.2	0.24	0.21	8.8	0.2	50.9	3.87	4.41	12.40	35.80	197	3.2
AIRC19_090	MM	0	171	7	34.7	2.43	123	0.8	4.6	0.32	69.00	7.9	1.19	34.5	2.42	4.79	12.30	33.90	171	
AIRC19_090	MM	0		9.6	37.5	3.60	118.6	0.83	4.3	0.41	34.53	8.91	0.93	34.5	3.31	5.90	12.50	35.80	237	2.54
AIRC19_090	MM	5	0	6.5	7.9	0.51	190	0.67	5.3	0.34	2.60	9	0.68	61.2	3.98	5.51	12.00	37.20	352	

AIRC19_091	MM	0		8.46	20.5	1.73	218.1	0.76	4.1	0.35	0.03	10.15	2.63	41.5	3.51	10.39	14.50	42.30	215	1.79
AIRC19_091	MM	2	55	6.5	13.9	0.90	218	0.66	3.7	0.24	0.11	9.4	0.31	55.9	3.63	5.55	12.20	36.90	306	
AIRC19_091	MM	5	95	6.9	6.1	0.42	186	0.63	3.8	0.26	0.20	9.9	0.34	62.4	4.31	0.36	13.70	38.80	31	
AIRC19_091	MM	10	3	6.6	5.7	0.38	212	0.64	3.8	0.25	0.83	9.6	0.1	64.4	4.25	3.83	12.90	37.50	218	
AIRC19_093	MM	0		6.87	1.3	0.09	208.9	0.92	3.3	0.23	0.00	9.86	0.36	68.6	4.71	5.76	14.30	41.80	130	3.12
AIRC19_093	MM	1	19	6.2	2	0.12	174	1.04	3.5	0.22		9.9	0.58	69.2	4.29	1.82	13.70	41.10	101	
AIRC19_093	MM	5	0	5.2	1.6	0.08	199	0.78	4.4	0.23	0.02	9.4	1.98	65.9	3.43	2.53	13.10	37.60	79	2.3
AIRC19_093	MM	10	1	7.3	x	x	230	0.95	3.6	0.26	0.17	9.9	0.20	67.8	4.95	7.71	13.20	37.20	114	

m=months; LDH=lactate dehydrogenase; β 2G=beta-2 globulin; CRP=C-reactive protein; WBC=white blood cell; β 2M=beta-2 microglobulin; x=positive not-quantifiable (>0 and <0.01)

Table S4. Reference ranges accounted for in our laboratory for biochemical parameters.

	Range Male	Range Female
Total Protein (g/dL)	6.6-8.3	6.6-8.3
Serum M-Protein (%)	absent	absent
Serum M-Protein (g/dL)	absent	absent
Lactate Dehydrogenase (IU/L)	<248	<248
Serum Creatinine (mg/dL)	0.6-1.3	0.6-1.3
Beta-2 Globulin (%)	11.1-18.8	11.1-18.8
Beta-2 Globulin (g/dL)	0.7-1.5	0.7-1.5
Kappa/Lambda Ratio	0.26-1.65	0.26-1.65
Calcium (mg/dL)	8.6-10.5	8.6-10.5
C-Reactive Protein (mg/dL)	<0.5	<0.5
Serum Albumin (%)	55.8-66.1	55.8-66.1
Serum Albumin (g/dL)	3.3-5.7	3.3-5.7
White Blood Cells (x10⁹/L)	3.6-10.5	3.6-10.5
Hemoglobin (g/dL)	13.5-17.2	12-15.6
Hematocrit (%)	39.5-50.5	35.5-45.5
Platelets (x10⁹/L)	160-370	160-370
Serum Beta-2 Microglobulin (mg/L)	0.7-1.8	0.7-1.8
Creatinine Clearance (ml/min)	97-137	88-128

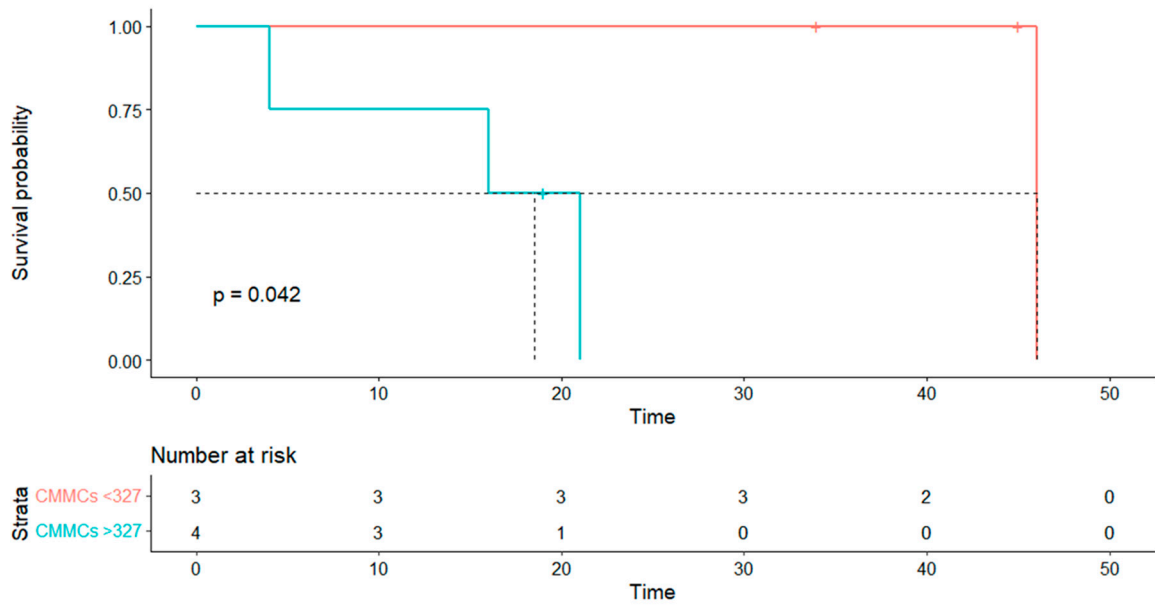
Table S5. BM NGS-based MRD measurements at different time-point for each patient and the relative CMMCs count.

Patient ID	Time-point post treatment (m)	Results	Quantifications	CMMCs count
AIRC19_082	3	NEG	0	0
AIRC19_081	4	NEG	0	0
AIRC19_083	4	POS	2.17E-04	0
AIRC19_038	6	NEG	0	0
AIRC19_029	6	POS	3.35E-03	0
AIRC19_082	10	NEG	0	0
AIRC19_083	10	POS	2.52E-04	0
AIRC19_004	10	POS	4.24E-04	0
AIRC19_018	11	NEG	0	0
AIRC19_033	11	NEG	0	0
AIRC19_029	11	POS	9.41E-03	0
AIRC19_020	12	NEG	0	0
AIRC19_083	13	POS	1.01E-05	0
AIRC19_012	14	POS	1.45E-03	0
AIRC19_060	15	NEG	0	0
AIRC19_036	16	NEG	0	0

AIRC19_035	16	POS	1.00E-05	0
AIRC19_035	19	POS	4.24E-05	0
AIRC19_056	6	POS	1.00E-05	1
AIRC19_014	7	POS	3.22E+00	1
AIRC19_016	8	NEG	0	1
AIRC19_060	8	NEG	0	1
AIRC19_028	11	NEG	0	1
AIRC19_028	18	POS	9.22E-05	1
AIRC19_026	24	NEG	0	2
AIRC19_019	7	POS	8.25E-05	3
AIRC19_091	12	POS	1.29E-02	3
AIRC19_039	11	POS	2.19E-03	4
AIRC19_026	9	NEG	0	5
AIRC19_026	11	NEG	0	5
AIRC19_030	11	NEG	0	6
AIRC19_024	6	POS	1.06E-03	8
AIRC19_014	10	POS	2.70E-03	8
AIRC19_019	10	POS	2.83E-05	12
AIRC19_057	13	NEG	0	12
AIRC19_054	19	NEG	0	19
AIRC19_054	9	POS	2.06E-03	28
AIRC19_020	7	POS	2.91E-03	31
AIRC19_088	10	POS	3.86E-03	39
AIRC19_085	10	POS	2.85E-03	68
AIRC19_091	6	POS	5.38E-03	95
AIRC19_055	16	POS	1.00E-05	619

m=months; POS=detectable MRD; NEG=undetectable MRD

A



B

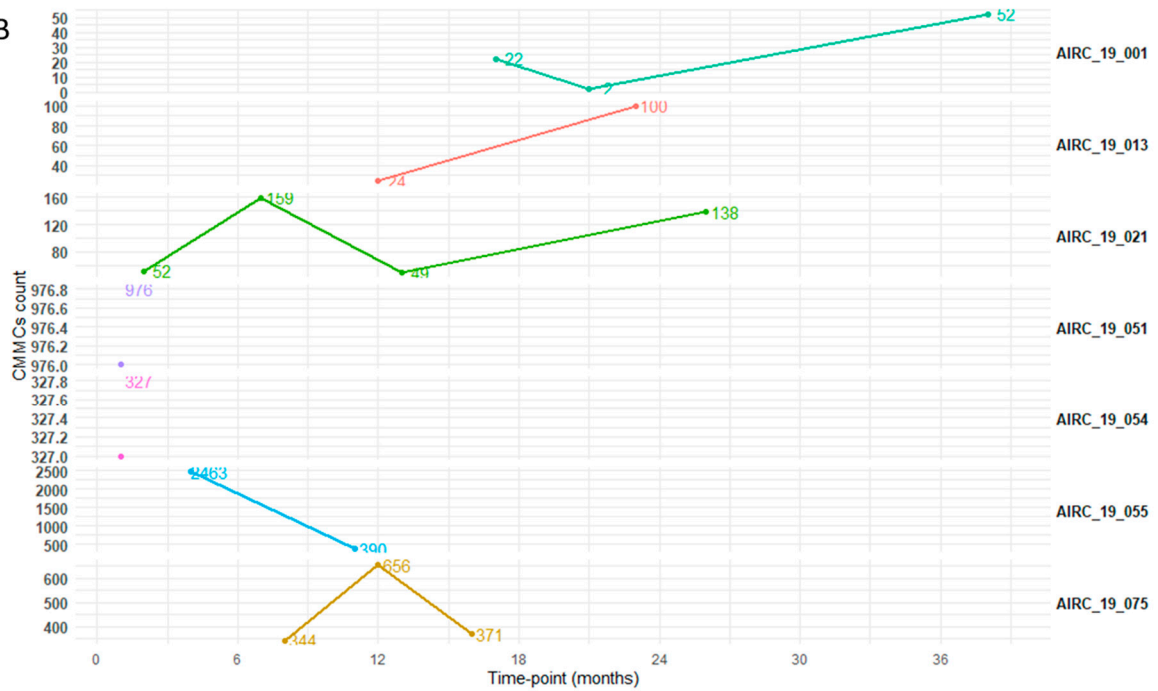


Figure S1. A) Time-to-progression to active MM according to CMMCs median basal levels ($p=0.042$). B) SMM line plot CMMCs kinetics highlighted *per patient*.



Figure S2. Line plot of CMMCs kinetics over time (in months) highlighted *per patient* in the context of coMMstant index=1.

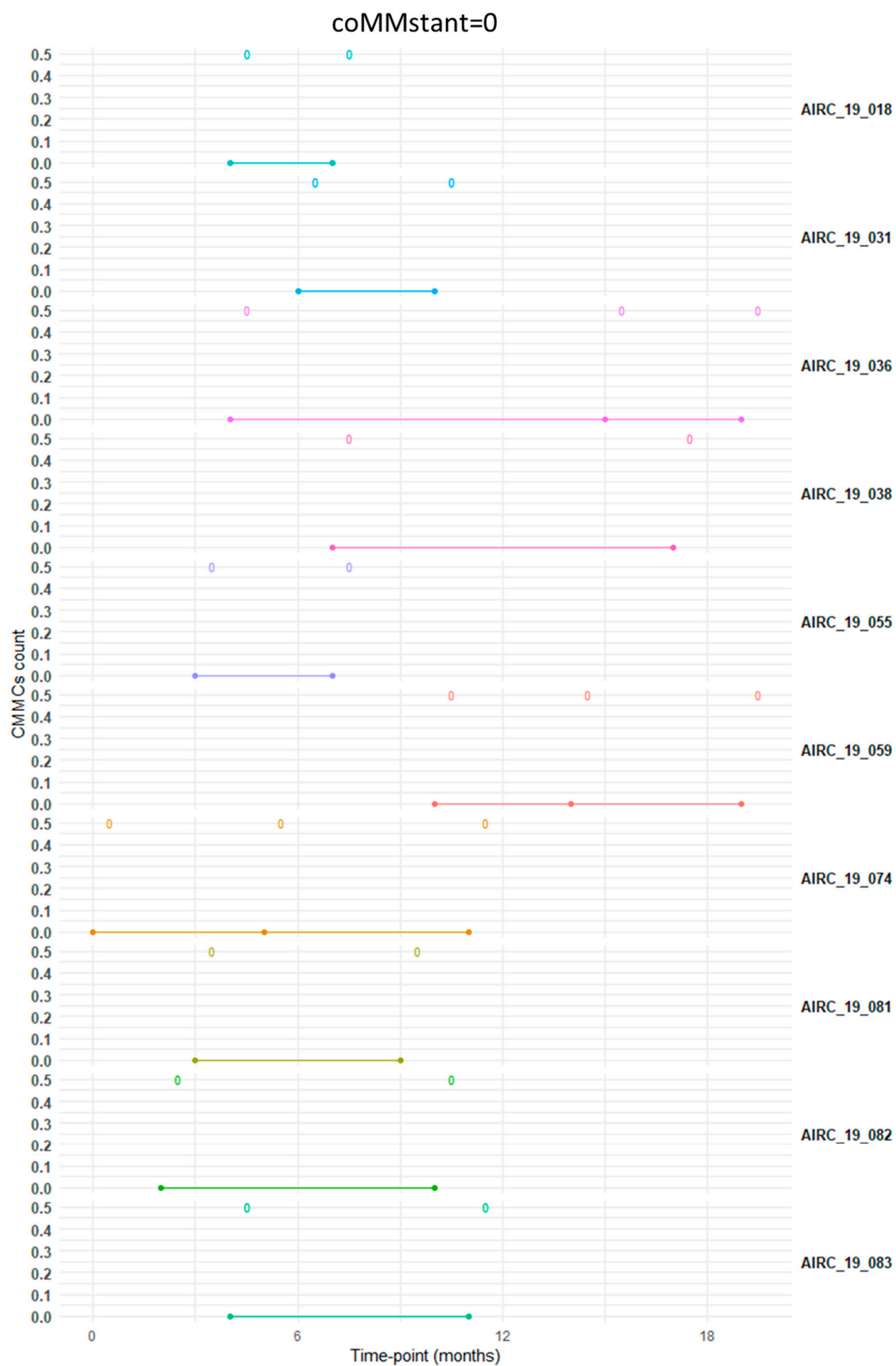


Figure S3. Line plot of CMMCs kinetics over time (in months) highlighted *per patient* in the context of coMMstant index=0.

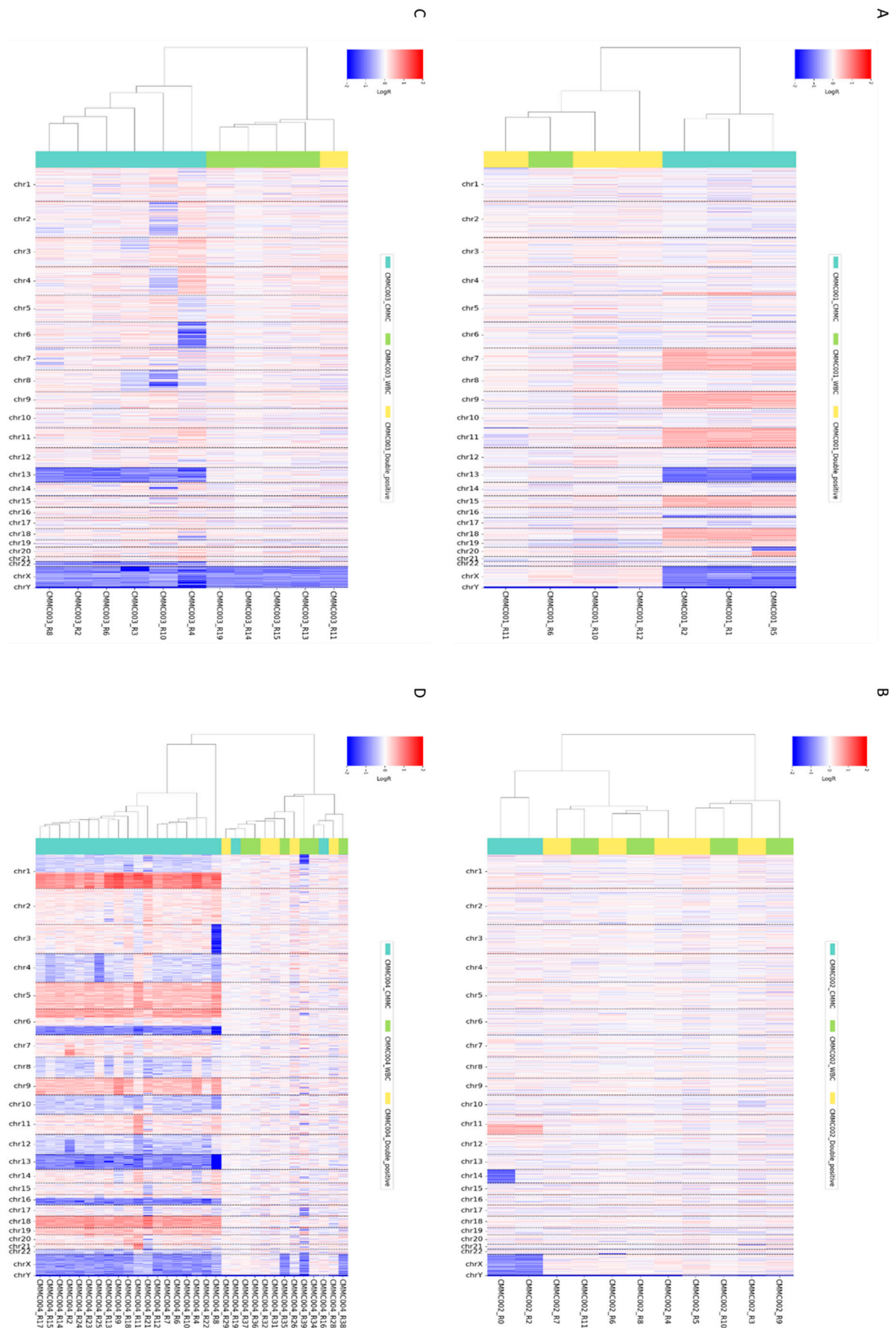


Figure S4. Heat-maps panel of CMMCs single-cell genomic analyses. A) Patient AIRC19_031 (CMMC1) CNAs profiles; B) AIRC19_24 (CMMC2); C) Patient AIRC19_28 (CMMC3) heat-map graph; D) Patient AIRC19_20 (i.e., CMMC4) CN variations profile. In blue deletions are displayed, while in red amplifications for each chromosome are analyzed.

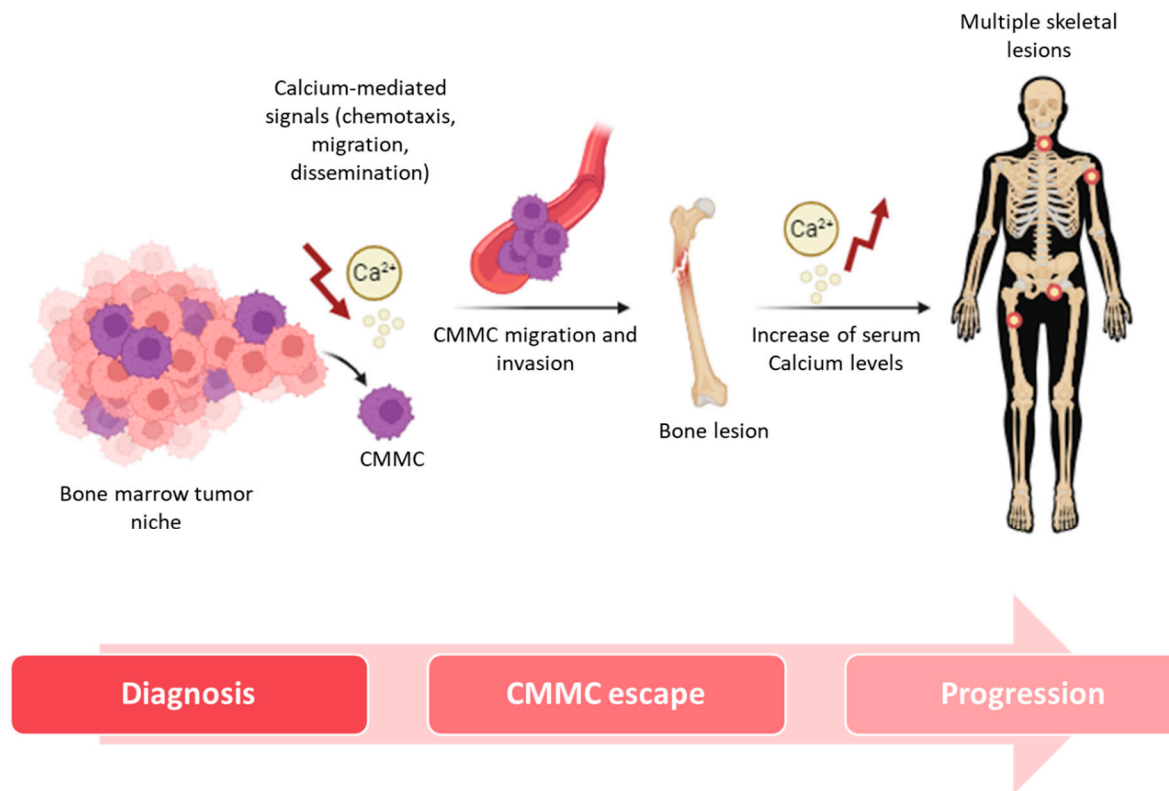


Figure S5. Schematic design of the CMMCs released from the BM niche, subsequent to a Calcium-induced pathway promoting chemotaxis and migration. CMMCs then colonize and induce bone lesions causing a subsequent increase in Calcium levels. Design was done by BioRender® (<https://app.biorender.com/>).