

Patient ID	Tissue biopsy	Liquid biopsy
Pt-1	Skin biopsy, right scapula- Month 12 (Stage IV)	Plasma (cfDNA2) - Month 22 (Stage IV)
	**PALB2 c.1317delG; p. F440fs*12 (43%) Loss/T2C	**PALB2 c.1317delG; p. F440fs*12 (51%) Loss/T2C RB1 splice 607+1 G>C (11%) Loss/T2C
Pt-2	Breast tissue biopsy - Month 33 (Stage IV)	Serum- Month 33 (Stage IV)
	**MSH2 c.1724A>G; p. D575G (51%) Normal TP53 c.721_722insA; p. S241fs*23 (16%) Loss/T2C	**MSH2 c.1724A>G; p. D575G (44%) Unknown TP53 c.721_722insA; p. S241fs*23 (5.59%) Loss/T2C
Pt-3	Cells from malignant pleural effusion -Month 12 (Stage IV)	Serum - Month 12 (Stage IV)
	**MUTYH c.1145G>A; p. G382D (44%) Loss/T3 TP53 c.375+1G>T (21%) Loss/T2C	**MUTYH c.1145G>A; p. G382D (43%) Loss/T3 TP53 c.375+1G>T (56%) Loss/T2C PMS2 c.89A>C; p.Q30P (2.97%) Loss/T2C
Pt-4	Skin breast biopsy- Month 17 (Stage IV)	Serum - Month 17 (Stage IV)
	**BRCA1 c.68_69delAG; p. E23fs*17 (50%) Loss/T1A	**BRCA1 c.68_69delAG; p. E23fs*17 (48%) Loss/T1A MSH6 c.3261delC; p. F1088fs*2 (2.92%) Loss/T2C
Pt-5	Skin upper arm biopsy- Month 13 (Stage IV)	Serum- Month 13 (Stage IV)
	**ESR1 c.805C>T; p. R269C (48%) Loss/T3	**ESR1 c.805C>T; p. R269C (50%) Loss/T3
Pt-6	Breast tissue- Month 3 (Stage IV)	Serum - Month 3 (Stage IV)
	***BRCA2 c.7976G>A; p. R2659K (50%) Loss/T1A MEN1 c.1471G>T; p. E491* (71%) Loss/T3	***BRCA2 c.7976G>A; p. R2659K (50%) Loss/T1A MRE11 c.1532delA; p. N511fs*13 (2.64%) Loss/T2C
Pt-7	Cells malignant pleural effusion-Month 25 (Stage IV)	Plasma- Month 21 (Stage IV)
	**KMT2C c.10432C>G; p. Q3478E (43%) Loss/T3 TP53 c.817C>T; p. R273C (58%) T2C	**KMT2C c.10432C>G; p. Q3478E (50%) Loss/T3 TP53 c.817C>T; p. R273C (6.77%) T2C MSH6 c.3261delC; p. F1088fs*2 (2.63%) Loss/T2C
Pt-8	Skin biopsy breast- Month 8 (Stage IV)	Plasma- Month 15 (Stage IV)
	**BARD1 c.2300_2301delTG; p. V767fs*4 (44%) Loss/T3 AR c.170T>A; p. L57Q (4.86%) Loss/T3	**BARD1 c.2300_2301delTG; p. V767fs*4 (41%) Loss/T3
Pt-9	Skin biopsy- Month 28 (Stage IV)	Plasma- Month 30 (Stage IV)
	**BRCA2 c.3975_3978dupTGCT; p. A1327fs*4 (50%) Loss/T1A	**BRCA2 c.3975_3978dupTGCT; p. A1327fs*4 (59%) Loss/T1A TP53 c.328delC; p. R110fs*13 (12%) Loss/T2C RB1 c.2158_2164delAAATTCAinsTGTAACAT; p.K720fs*31 (9.4%)

		Loss/T3
Pt-10	Lymph node- Month 9 (Stage IV)	Plasma - Month 9 (Stage IV)
	TP53 c.329delG; p. R110fs*13 (74%) Loss/T2C	TP53 c.329delG; p. R110fs*13 (19%) Loss/T2C
Pt-11	Skin from chest wall- Month 21 (Stage IV)	Plasma- Month 23 (Stage IV)
	**RAD51C c.428A>G; p. Q143R (79%) Loss/T2C **AR c.2395C>G; p. Q799E (72%) Loss/T3 TP53 c.686_687delGT; p. C229fs*10 (48%) Loss/T2C ERBB2 c.2329G>T; p. V777L (54%) Gain/T2C ERBB2 c.929C>T; p. S310F (55%) Gain/T2C PIK3CA c.331A>G; p. K111E (38%) Gain/T2C	**RAD51C c.428A>G; p. Q143R (56%) Loss/T2C **AR c.2395C>G; p. Q799E (51%) Loss/T3 TP53 c.686_687delGT; p. C229fs*10 (13%) Loss/T2C ERBB2 c.2329G>T; p. V777L (6.71%) Gain/T2C ERBB2 c.929C>T; p. S310F (9.59%) Gain/T2C PIK3CA c.331A>G; p. K111E (9.05%) Gain/T2C
Pt-12	Skin biopsy- Month 27 (Stage IV)	Serum - Month 27 (Stage IV)
	PTEN c.30_41delCAGAAACAAAAG; p. S10_K13del (69%) Loss/T2C PMS1 c.2153T>G; p. L718* (80%) Loss/T2C BAP1 c.680G>C; p. R227P (72%) Loss/T2C	PTEN c.30_41delCAGAAACAAAAG; p. S10_K13del (6.1%) Loss/T2C PMS1 c.2153T>G; p. L718* (4.9%) Loss/T2C BAP1 c.680G>C; p. R227P (2.84%) Loss/T2C TP53 c.292_315delCCTTCCCAGAAAACCTACCAGGGCinsAG p. P98fs*18 (5.29% of 1438) T2C
Pt-13	NO tumor tissue available	Plasma- Month 9 (Stage IV)
		**FANCC c.823T>C; p. F275L (55%) Loss/T3 TP53 c.499C>T; p. Q167* (5.06%) Loss/T2C MSH6 c.3261delC; p. F1088fs*2 (2%) Loss/T2C
Pt-14	Breast tissue- Month 7 (Stage III)	Plasma – Month 10 (Stage III)
	PTEN c.968dupA; p. N323fs*2 (12%) Loss/T2C PIK3R1 c.1102delT; p. Y368fs*5 (12%) T2C PIK3R1 c.1709_1735delTTATCCAGCTGAGAAAGACGAGAGACC p. L570_D578del (6.89%) T2C	PTEN c.968dupA; p. N323fs*2 (3.95%) Loss/T2C AR c.170T>A; p. L57Q (3.44%) Loss T3 KMT2C c.906T>A; p. C302* (4.19%) Loss/T3 PIK3R1 c.1362_1364dupTCA; p. T454_Q455insH (3.04%) Loss/T2C
Pt-15	Skin breast biopsy- Month 1 (Stage III)	Plasma - Month 1 (Stage III)
	TP53 c.375G>C; p. T125T (3.37%) Loss/T3	TP53 c.375G>C; p. T125T (30%) Loss/T3
Pt-16	Cells from malignant fluid abdomen - Month 44 (Stage IV)	Serum- Month 44 (Stage IV)
	RB1 c.2336T>A; p. L779* (89%) Loss/T3 TP53 c.294_310delTTCCCAGAAAACCTACC; p. S99fs*44 (83%)	RB1 c.2336T>A; p. L779* (24%) Loss/T3 TP53 c.294_310delTTCCCAGAAAACCTACC; p. S99fs*44 (23%)

	Loss/T2C PMS2 c.1239delA; p. D414fs*34 (2%) Loss/T2C	Loss/T2C PMS2 c.1239delA; p. D414fs*34 (2.5%) Loss/T2C
Pt-17	Skin chest wall- Month 35 (Stage IV)	Serum- Month 35 (Stage IV)
	TP53 c.690_702delCACCATCCACTAC; p. I232fs*11 (56%) Loss/T2C BRCA1 c.5278-1G>T (33%) Loss/T1A	TP53 c.690_702delCACCATCCACTAC; p. I232fs*11 (21%) Loss/T2C BRCA1 c.5278-1G>T (9.1%) Loss/T1A PMS2 c.89A>C; p. Q30P (2%) T2C
Pt-18	Breast tumor tissue- Month 15 (Stage IV)	Plasma- Month 15 (Stage IV)
	RETc.2071G>A; p. G691S (99%) Gain/T3 TP53 c.1024C>T; p. R342 (41%) Loss/T2C EGFR c.2281G>A; p. D761N (3.2%) Gain/T2C ATM c.8287C>T; p. R2763* (2.1%) Loss/T2C (2.1%)	*RETc.2071G>A; p. G691S (100%) Gain/T3 TP53 c.1024C>T; p. R342* (3.21%) Loss/T2C

Table S1. Germline and somatic variants in triple negative IBC. Clinically relevant germline and somatic variants are shown. Time of collection from disease onset and stage of the disease at the time of sample collection are indicated in each case. For each variant, its allele fraction (AF) is indicated in parenthesis. The variants were classified according their pathogenicity as pathogenic (in red), likely pathogenic (in blue), or variants of uncertain significance (in black). Variants were also classified according to its actionability: T1A indicates strong clinical significance; T2C indicates potential clinical significance and FDA-approved therapies for different tumor types or investigational therapies; T3 indicates biomarker is of uncertain clinical significance. Loss or gain of protein functions are indicated. **Germline variants confirmed by NGS of whole blood or normal tissue. ***Germline variant according to clinical test in patient clinical history file. For Pt-1, cfDNA samples from month 12 (cfDNA1) and month 22 (cfDNA2) were studied, and *PALB2* variant was detected in both, but the *RBI* mutation was only detected in cfDNA from month 22. Protein loss or gain of function is indicated for some variants.