

SUPPLEMENTARY TABLES

Supplementary table 1. Search Strategy.

Search	Query	Results
#12	Search: " multiple different molecular classif* " endometrial Sort by: Publication Date	21
#11	Search: " multiple classifier " endometrial Sort by: Publication Date	2
#10	Search: " multiple molecular marker* " endometrial [Title/Abstract] Sortby: Publication Date	1
#8	Search: (("Endometrial Neoplasms"[Mesh]) AND (multiple[Title/Abstract])) AND (classif*[Title/Abstract]) Sort by: Publication Date	81
#7	Search: ("Endometrial Neoplasms/classification"[Mesh]) AND(multiple[Title/Abstract]) Sort by: Publication Date	12
#6	Search: endometrial " multiple classifier "[Title/Abstract] Sort by: Publication Date	2
#4	Search: " Endometrial Neoplasms "[Mesh] Sort by: Most Recent	24,670
#3	Search: " Endometrial Neoplasms/classification "[Mesh] Filters: in the last 10 years, English Sort by: Most Recent	171
#2	Search: " Endometrial Neoplasms/classification "[Mesh] Filters: English Sort by: Most Recent	311
#1	Search: " Endometrial Neoplasms/classification "[Mesh] Sort by: MostRecent	354
#0	Search: Clipboard	192

Supplementary table 2. Clinicopathologic and molecular characteristics of multiple classifiers.

Molecular class	Age	Histology	Grade	Stage	MI	LN	LVISI	Risk class	MSI	MMR IHC	MLH1	PMS2	MSH6	MSH2	POLE	TP53 NGS	P53 IHC
MMRd-p53abn	55	Endometrioid	Grade 1	IA	None	Neg	Absent/Focal	Low	MSI	MMRd	+	+	-	+	WT	Mut	WT
MMRd-p53abn	59	Endometrioid	Grade 1	IA	<50%	Neg	Absent/Focal	Low	MSI	MMRd	-	-	+	+	WT	Mut	Na
MMRd-p53abn	56	Endometrioid	Grade 1	IA	<50%	Neg	Absent/Focal	Low	Na	MMRd	+	+	-	+	WT	Mut	aberrant
MMRd-p53abn	54	Endometrioid	Grade 1	IA	<50%	Neg	Absent/Focal	Low	MSI	MMRd	-	-	+	+	WT	Mut	Na
MMRd-p53abn	74	Endometrioid	Grade 2	IA	<50%	Neg	Absent/Focal	Low	MSI	MMRd	-	-	+	+	WT	Mut	aberrant
MMRd-p53abn	64	Endometrioid	Grade 2	IA	<50%	Neg	Absent/Focal	Low	MSI	MMRd	-	-	+	+	WT	WT	aberrant
MMRd-p53abn	72	Endometrioid	Grade 2	IA	<50%	Neg	Absent/Focal	Low	MSI	MMRd	+	+	-	+	WT	Mut	Na
MMRd-p53abn	69	Clear cell	Grade 3	IA	None	Neg	Absent/Focal	Intermediate	MSS	MMRd	+	+	-	+	WT	Mut	aberrant
MMRd-p53abn	78	Endometrioid	Grade 3	IA	None	Neg	Absent/Focal	Intermediate	MSI	MMRd	+	+	-	+	WT	Mut	aberrant
MMRd-p53abn	55	Endometrioid	Grade 3	IA	<50%	Neg	Absent/Focal	Intermediate	MSI	MMRd	+	+	Patchy	-	WT	Mut	aberrant
MMRd-p53abn	55	Endometrioid	Grade 3	IA	<50%	Neg	Absent/Focal	Intermediate	MSI	MMRd	+	+	-	-	WT	Mut	aberrant
MMRd-p53abn	75	Endometrioid	Grade 3	IA	<50%	Neg	Absent/Focal	Intermediate	MSI	MMRd	-	-	+	+	WT	WT	aberrant
MMRd-p53abn	55	Endometrioid	Grade 3	IA	<50%	Neg	Absent/Focal	Intermediate	Na	MMRd	+	+	-	+	WT	Mut	subclonal
MMRd-p53abn	84	Serous	Grade 3	IA	None	Neg	Absent/Focal	Intermediate	MSI	MMRd	+	+	-	+	WT	Mut	aberrant
MMRd-p53abn	82	Endometrioid	Grade 2	IB	≥50%	Neg	Absent/Focal	Intermediate	MSI	MMRd	-	-	+	+	WT	Mut	WT
MMRd-p53abn	74	Endometrioid	Grade 3	IB	≥50%	Neg	Diffuse	High-intermediate	MSI	MMRd	+	+	-	Patchy	WT	Mut	aberrant
MMRd-p53abn	50	Endometrioid	Grade 2	II	<50%	Neg	Absent/Focal	High-intermediate	MSS	MMRd	+	+	-	+	WT	Mut	aberrant
MMRd-p53abn	55	Endometrioid	Grade 3	II	<50%	Neg	Absent/Focal	High-intermediate	MSI	MMRd	-	-	-	+	WT	Mut	WT
MMRd-p53abn	50	Mixed	Grade 3	IA	<50%	Neg	Diffuse	High	MSI	MMRd	+	+	-	-	WT	Mut	WT
MMRd-p53abn	69	Endometrioid	Grade 2	IIIA	≥50%	ITC	Absent/Focal	High	MSI	MMRd	+	+	-	-	WT	Mut	Na
MMRd-p53abn	46	Endometrioid	Grade 3	IIIA	<50%	Neg	Absent/Focal	High	MSI	MMRd	+	+	-	+	WT	Mut	subclonal
MMRd-p53abn	50	Endometrioid	Grade 2	IIIC1	<50%	Micro/Macro	Absent/Focal	High	MSI	MMRd	-	-	+	+	WT	Mut	subclonal
MMRd-p53abn	63	Endometrioid	Grade 2	IIIC1	<50%	Micro/Macro	Diffuse	High	MSI	MMRd	-	-	+	+	WT	WT	aberrant
MMRd-p53abn	54	Endometrioid	Grade 3	IIIC1	≥50%	Micro/Macro	Absent/Focal	High	MSI	MMRd	-	-	+	+	WT	Mut	Na
MMRd-p53abn	76	Undifferentiated	Undifferentiated	IIIC1	≥50%	Micro/Macro	Diffuse	High	MSI	MMRd	-	-	+	+	WT	WT	aberrant
MMRd-p53abn	60	Endometrioid	Grade 3	IIIC2	≥50%	Micro/Macro	Diffuse	High	MSI	MMRd	+	+	-	+	WT	Mut	subclonal
MMRd-p53abn	63	Endometrioid	Grade 3	IVB	≥50%	Micro/Macro	Absent/Focal	Advanced/metastatic	MSI	MMRd	-	-	+	+	WT	Mut	aberrant
MMRd-p53abn	67	Other	Na	IVB	Na	Na	Na	Advanced/metastatic	MSI	Na	Na	Na	Na	Na	WT	Mut	Na
POLE-P53abn	44	Endometrioid	Grade 1	IA	None	Neg	Absent/Focal	Low	MSS	MMRp	+	+	+	+	Mut	Mut	aberrant
POLE-P53abn	54	Endometrioid	Grade 1	IA	None	Neg	Absent/Focal	Low	MSS	MMRp	+	+	+	+	Mut	Mut	subclonal
POLE-P53abn	59	Endometrioid	Grade 2	IA	None	Neg	Absent/Focal	Low	MSS	MMRp	+	+	+	+	Mut	WT	aberrant
POLE-P53abn	57	Endometrioid	Grade 2	IA	<50%	Neg	Absent/Focal	Low	MSS	Na	Na	Na	Na	Na	Mut	Mut	Na
POLE-P53abn	59	Endometrioid	Grade 2	IA	<50%	Neg	Absent/Focal	Low	MSS	Equivocal	+	+	Patchy	+	Mut	Mut	aberrant
POLE-P53abn	44	Endometrioid	Grade 3	IA	None	Neg	Absent/Focal	Intermediate	Na	MMRp	+	+	+	+	Mut	Mut	WT
POLE-P53abn	51	Endometrioid	Grade 3	IA	None	Neg	Absent/Focal	Intermediate	MSS	Equivocal	+	+	Patchy	Patchy	Mut	Mut	aberrant
POLE-P53abn	79	Endometrioid	Grade 3	IA	<50%	Neg	Absent/Focal	Intermediate	Na	MMRp	+	+	+	+	Mut	Mut	subclonal
POLE-P53abn	57	Endometrioid	Grade 3	IA	<50%	Na	Absent/Focal	Intermediate	MSS	MMRp	+	+	+	+	Mut	Mut	Na
POLE-P53abn	58	Endometrioid	Grade 3	IA	<50%	Neg	Absent/Focal	Intermediate	MSS	MMRp	+	+	+	+	Mut	Mut	subclonal
POLE-P53abn	42	Endometrioid	Grade 3	IB	≥50%	Na	Absent/Focal	High-intermediate	Na	MMRp	+	+	+	+	Mut	Mut	subclonal

POLE-P53abn	75	Endometrioid	Grade 3	IB	≥50%	Neg	Absent/Focal	High-intermediate	MSS	MMRp	+	+	+	+	Mut	Mut	WT
POLE-P53abn	44	Endometrioid	Grade 3	IB	≥50%	Neg	Absent/Focal	High-intermediate	MSS	Na	Na	Na	Na	Na	Mut	Mut	Na
POLE-P53abn	59	Clear cell	Grade 3	IB	≥50%	Neg	Diffuse	High	MSS	MMRp	+	+	+	+	Mut	Mut	WT
POLE-P53abn	59	Endometrioid	Grade 3	IIIA	≥50%	Neg	Absent/Focal	High	MSS	MMRp	+	+	+	+	Mut	Mut	aberrant
POLE-MMRd	47	Endometrioid	Grade 1	IA	<50%	Neg	Absent/Focal	Low	MSI	MMRd	+	+	-	+	Mut	WT	Na
POLE-MMRd	47	Endometrioid	Grade 2	IA	<50%	ITC	Absent/Focal	Low	MSS	MMRd	-	-	+	+	Mut	WT	Na
triple positive	59	Endometrioid	Grade 3	IA	<50%	Neg	Absent/Focal	Intermediate	MSS	MMRd	+	+	-	+	Mut	Mut	subclonal
triple positive	54	Endometrioid	Grade 3	IB	≥50%	Neg	Absent/Focal	High-intermediate	MSI	MMRd	-	-	Patchy	+	Mut	Mut	aberrant
triple positive	51	Mixed	Grade 3	IB	≥50%	Neg	Absent/Focal	High	MSI	MMRd	+	+	-	+	Mut	Mut	aberrant

Abbreviations: Na, not available. Notes: +, normal expression (positive, present); -, loss of expression (negative, absent)

Supplementary table 3. Discordance between TP53 next generation sequencing and p53 immunohistochemistry.

p53 IHC - TP53 NGS discordance		Single classifier N=327	Multiple classifier N=37
Concordant	IHC normal - NGS wild type	235 (71.9%)	0 (0.0%)
	IHC aberrant - NGS mutated	60 (18.4%)	25 (67.6%)
Discordant	IHC aberrant - NGS wild type	28 (8.6%)	5 (13.5%)
	IHC normal - NGS mutated	4 (1.2%)	7 (18.9%)

Abbreviations: IHC, immunohistochemistry; NGS, next-generation sequencing

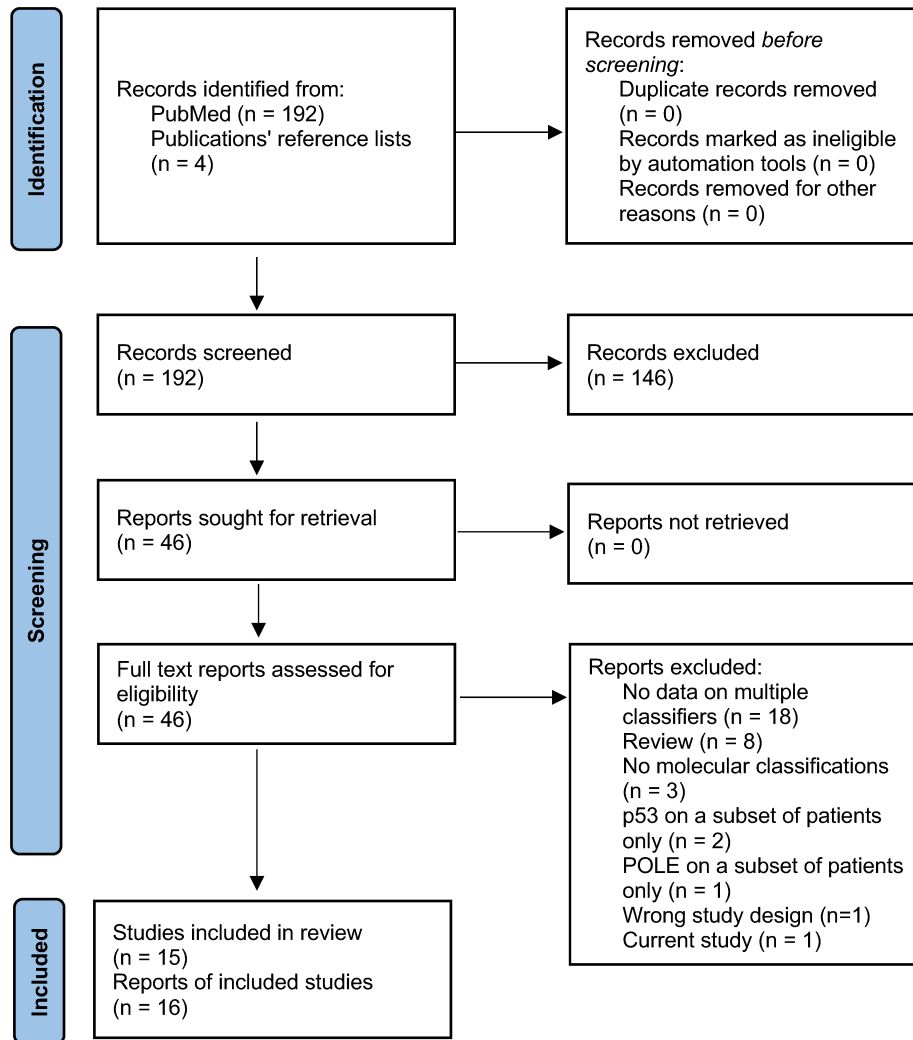
Supplementary table 4. Discordance between microsatellite instability assay and MMR protein immunohistochemistry.

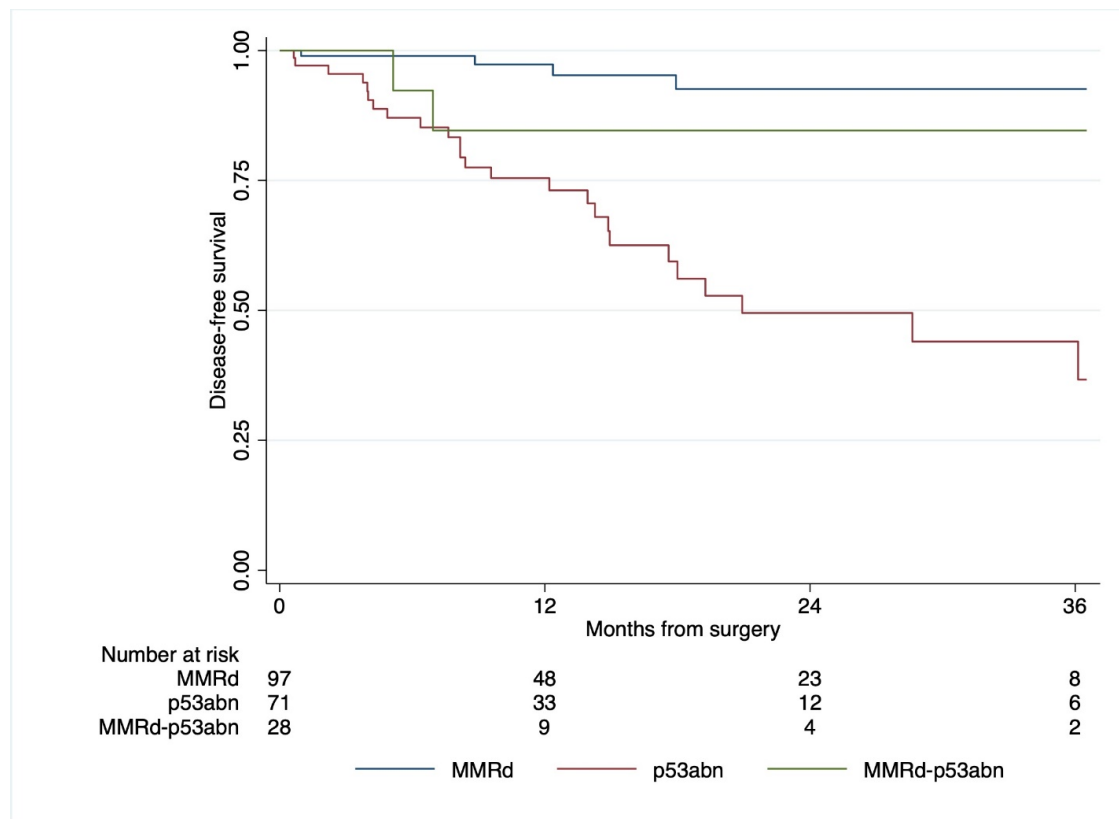
MMR IHC - MSI assay discordance		Single classifier N=355	Multiple classifier N=40
Concordant	MMRp - MSS	260 (73.2%)	10 (25.0%)
	MMRd - MSI	79 (22.3%)	26 (65.0%)
Discordant	MMRd - MSS	11 (3.1%)	4 (10.0%)
	MMRp - MSI	5 (1.4%)	0 (0.0%)

Abbreviations: IHC, immunohistochemistry; MMR, mismatch repair protein; MMRp, MMR proficient; MMRd, MMR deficient; MSI, microsatellite instable; MSS, microsatellite stable.

SUPPLEMENTARY FIGURES

Supplementary figure 1. Study flow diagram.



Supplementary figure 2. Kaplan-Meier curves of MMRd, p53abn, and MMRd-p53abn.

Supplementary figure 3. Kaplan-Meier curves of POLEmut, p53abn, and POLEmut-p53abn.