Impact of Endometrial Cancer Molecular Profiling on Emerging Treatment Landscape

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SEOUL IGCS 2023

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Two Year Disclosure of Financial Relationships for Dr. Bradley Monk Oct 2023

Sponsors involved in producing, marketing, selling, re-selling, or distributing products

Cancer Type	Commercial Interest	What was received	Role
Cervical, uterine, ovarian	AstraZeneca	Honorarium	Speaker/Consultant
Uterine, ovarian	Eisai	Honorarium	Speaker/Consultant
Cervical, uterine, ovarian	Genmab/Seagen	Honorarium	Consultant
Ovarian	ImmunoGen	Honorarium	Speaker/Consultant
Uterine	Karyopharm	Honorarium	Consultant
Cervical, uterine, ovarian	Merck	Honorarium	Speaker/Consultant
Cervical, uterine, ovarian	Myriad	Honorarium	Speaker/Consultant
Ovarian	Novocure	Honorarium	Consultant
Ovarian	Roche/Genentech	Honorarium	Speaker/Consultant
Cervical, uterine, ovarian	TESARO/GSK	Honorarium	Speaker/Consultant

Stock: None

Government or ineligible company employment: None

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Outline

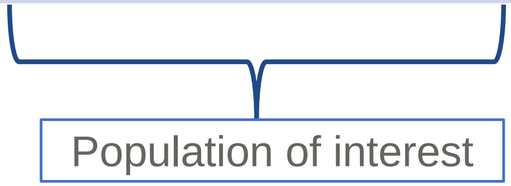
- **Broad overview of the molecular landscape of endometrial cancer**

- **Significant molecular subtypes**
  - *POLE*, MSI-h, copy number alterations, TMB, PD-L1
  - HER-2, ER/PR
  - TP53
  - Testing for molecular alterations – Which? When? How?

- **Clinical implications**
  - 2023 FIGO Staging
  - Guidelines
  - Eligibility for clinical trials

Estimated USA Endometrial Cancer 2023

> 59,000 new cases*		>11,000 deaths*
49,000 endometrioid		8,000
43,000	Grade 1-2	4.000
17,000	Grade 3	4,000
8,000 Serous		2,000
1,000 Clear cell		300
1,000 Carcinosarcoma		700



- * SEER 22 (Excluding IL/MA) 2013–2019, All Races, Females by SEER Combined Summary Stage.
- **SEER**, Surveillance, Epidemiology, and End Results Program.
- **1.** American Cancer Society. *Cancer Facts & Figures 2023*. American Cancer Society; 2023. **2.** National Cancer Institute. SEER cancer stat facts: uterine cancer. Accessed June 2, 2023. https://seer.cancer.gov/statfacts/html/corp.html

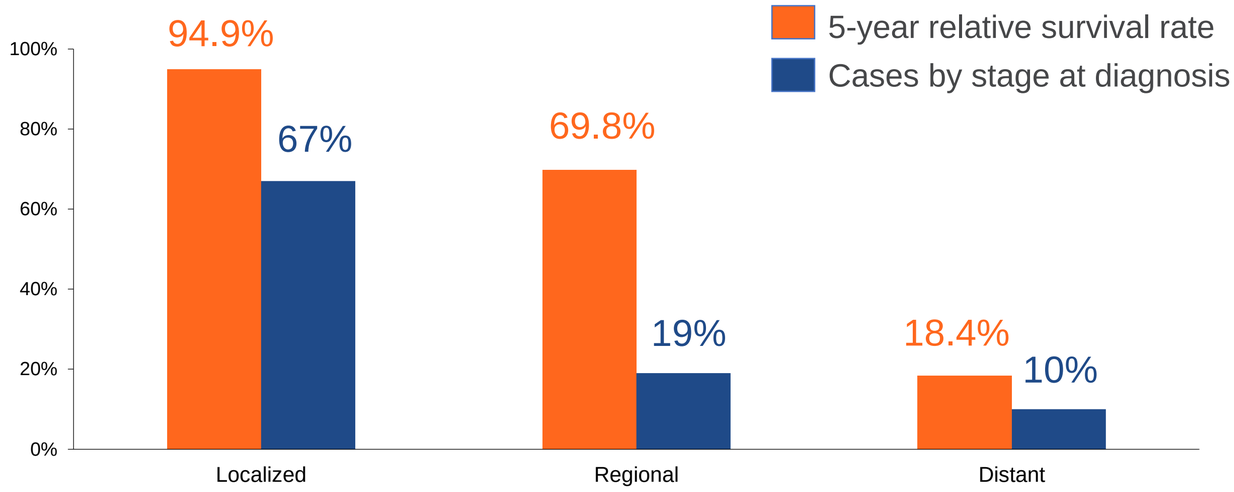
Endometrial Cancer Is the Most Common Gynecologic Malignancy in the US, With the Second Highest Mortality Rate[1]

In 2023[1]:

>59,000 new diagnoses

>11,000 deaths

5-Year Relative Survival Rate and Percentage of Cases by Stage at Diagnosis in Uterine Cancer[2]*



Although most patients are diagnosed with localized disease, those with advanced disease and high risk histologies typically have a poor prognosis[2]

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* SEER 22 (Excluding IL/MA) 2013–2019, All Races, Females by SEER Combined Summary Stage.

SEER, Surveillance, Epidemiology, and End Results Program.

1. American Cancer Society. *Cancer Facts & Figures 2023*. American Cancer Society; 2023. **2.** National Cancer Institute. SEER cancer stat facts: uterine cancer. Accessed June 2, 2023. https://seer.cancer.gov/statfacts/html/corp.html

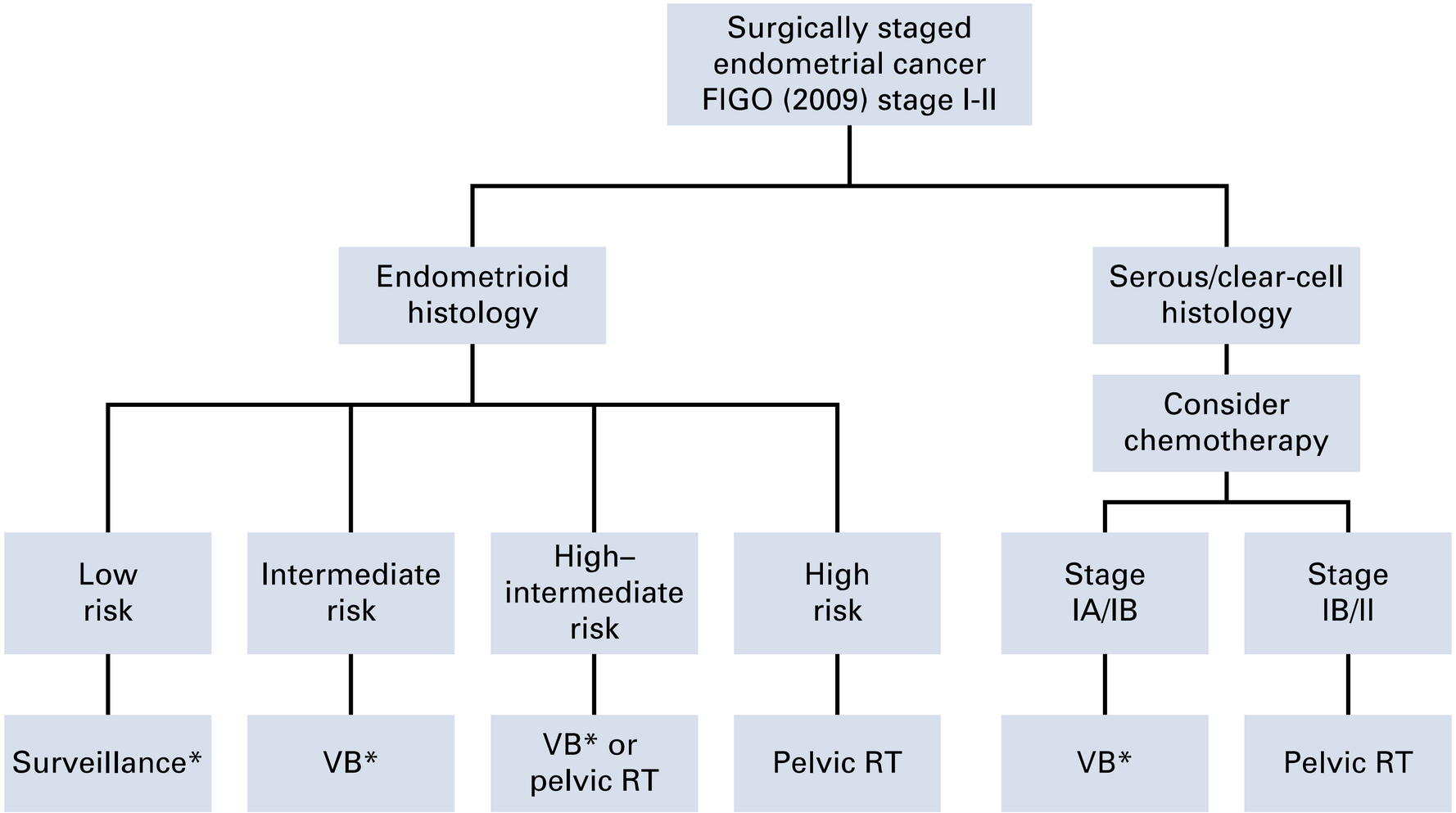
External Beam, Brachytherapy, or Chemotherapy? Defining Adjuvant Therapy for Early-Stage and High- and High-Intermediate-Risk Endometrial Cancer.

Risk category	Definition
Low risk	Grade 1-2, < 50% MMI
Intermediate risk	Grade 3, < 50% MMI OR Grade 1-2, ≥ 50% MMI, not fitting criteria for high–intermediate-risk disease
High–intermediate risk	≥ 70 years with 1 risk factor; or ≥ 50 years with 2 risk factors; or < 50 years with 3 risk factors Risk factors: Grade 2-3 disease, LVI, ≥ 50% MMI
High risk	Grade 3, ≥ 50% MMI; or Cervical stromal involvement

FIGO International Federation of Gynecology and Obstetrics; LVI, lymphovascular invasion; MMI, myometrial invasion; RT, radiation therapy; VB, vaginal brachytherapy.

Jang JW, Lee LJ.J Clin Oncol. 2019 Jul 20;37(21):1778-1784.

External Beam, Brachytherapy, or Chemotherapy? Defining Adjuvant Therapy for Early-Stage and High- and High-Intermediate-Risk Endometrial Cancer.



FIGO International Federation of Gynecology and Obstetrics; LVI, lymphovascular invasion; MMI, myometrial invasion; RT, radiation therapy; VB, vaginal brachytherapy.

(*) Consider treatment intensification (surveillance to VB, or VB to pelvic RT) depending on the presence of risk factors for vaginal and/or nodal recurrence, status of nodal assessment, extensive LVI, patient co-morbidity, and risk of radiation toxicity or complication

Jang JW, Lee LJ.J Clin Oncol. 2019 Jul 20;37(21):1778-1784.

Endometrial Cancer Has Traditionally Been Classified into 2 Pathological Types

- Type I endometrial cancer is typically associated with good prognosis, while type II is associated with poor prognosis[1]

Characteristics of Type I and Type II Endometrial Cancers[2,3]

Characteristic	Type I	Type II
Histology	Endometrioid	Non-endometrioid (serous, clear-cell, undifferentiated including carcinosarcomas)[3,4]
Grade	Usually low	Usually high
Stage	Often early	Often advanced
Etiology	Unopposed estrogen	Sporadic
Hormone receptor expression	Positive	Negative
Genomic stability[3]	Diploid, frequent MSI	Aneuploid
Common mutations	*PTEN*	*p53*

These classifications have been used for the past 3 decades, but they do not fully capture the wide range of clinical, genetic, and molecular characteristics of endometrial cancers[1]

MSI = microsatellite instability.

1. Morice P, et al. *Lancet.* 2016;387:1094-108. 2. Llobet D, et al. *J Clin Pathol.* 2009;62:777-85. 3. Binder PS, et al. *Women's Health (Lond).* 2014;10:277-88.
4. Remmerie M, et al. *Int J Mol Sci.* 2018;19:2380.

Endometrioid Endometrial Cancers Can Be Further Categorized Based on Molecular Profile

An integrated genomic analysis by The Cancer Genome Atlas (TCGA) network classified endometrioid endometrial cancers into 4 categories[1]

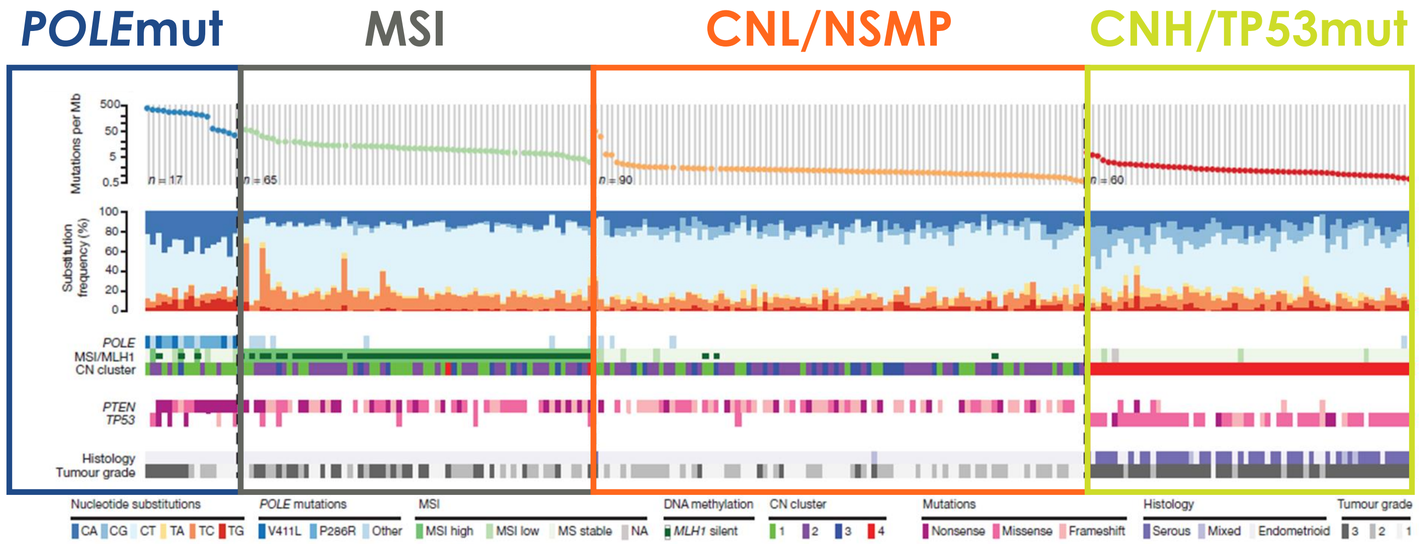
***POLE* ultramutated**	• Ultra-high somatic mutation frequency; MSS; frequent mutations in the exonuclease domain of *POLE*; high ASNS and CCNB1 expression • Represents ~4% of endometrioid tumors* • Best prognosis
MSI hypermutated	• High mutation rate and few copy number alterations; high rate of *MLH1* promoter methylation; high phospho-AKT; low PTEN expression; frequent *PIK3CA* and *PIK3R1* mutations co-occurring with *PTEN* mutations • Represents ~39% of endometrioid tumors*†
Copy-number low‡	• High frequency of mutations in *CTNNB1*, *KRAS*, *SOX17*; frequent *PIK3CA* and *PIK3R1* mutations co-occurring with *PTEN* mutations; elevated levels of progesterone receptor and RAD50 expression • Represents ~49% of endometrioid tumors*
Copy-number high‡	• Greatest transcriptional activity; frequent *TP53* mutations; decreased levels of phospho-AKT; mutually exclusive *PIK3CA*, *PIK3R1,* and *PTEN* mutations • Represents ~9% of endometrioid tumors* • Worst prognosis

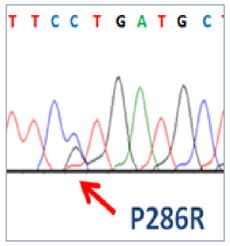
* The frequency of each molecular subgroup among endometrioid tumors was calculated in a follow-up study using a clinically applicable molecular classification system derived from the TCGA study.[2] † Tumors were classified as dMMR based on MSI and/or IHC defects. ‡ Tumors were clustered into low or high copy number groups based on the extent of somatic copy number alterations.

AKT, serine/threonine kinase; ASNS, asparagine synthetase (glutamine-hydrolyzing); CCNB1, cyclin B1; CTNNB1, catenin β1; dMMR, deficient mismatch repair; IHC, immunohistochemistry; KRAS, Kirsten rat sarcoma viral oncogene; MLH1, mutL homolog 1; MSI, microsatellite instability; MSS, microsatellite stable; phospho-AKT, phosphorylated AKT; PIK3CA; phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; PIK3R1, phosphoinositide-3-kinase regulatory subunit 1; POLE, polymerase ε; PTEN, phosphatase and tensin homolog; RAD50, RAD50 double-strand break repair protein; SOX17, SRY-box 17; TCGA, The Cancer Genome Atlas; TP53, tumor protein 53.

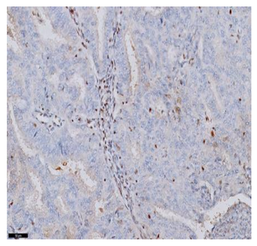
1. Cancer Genome Atlas Research Network. *Nature.* 2013;497:67-73. 2. Cosgrove CM, et al. *Gynecol Oncol.* 2018;148:174-80.

Most endometrial tumors can be classified into 1 of 4 molecular subgroups that are also prognostic[1,2]

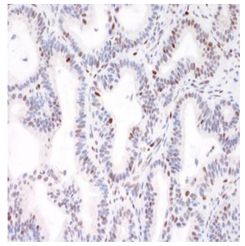




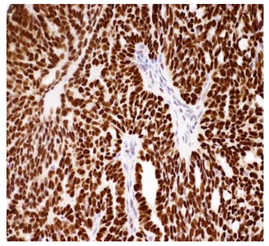
POLEmut



dMMR

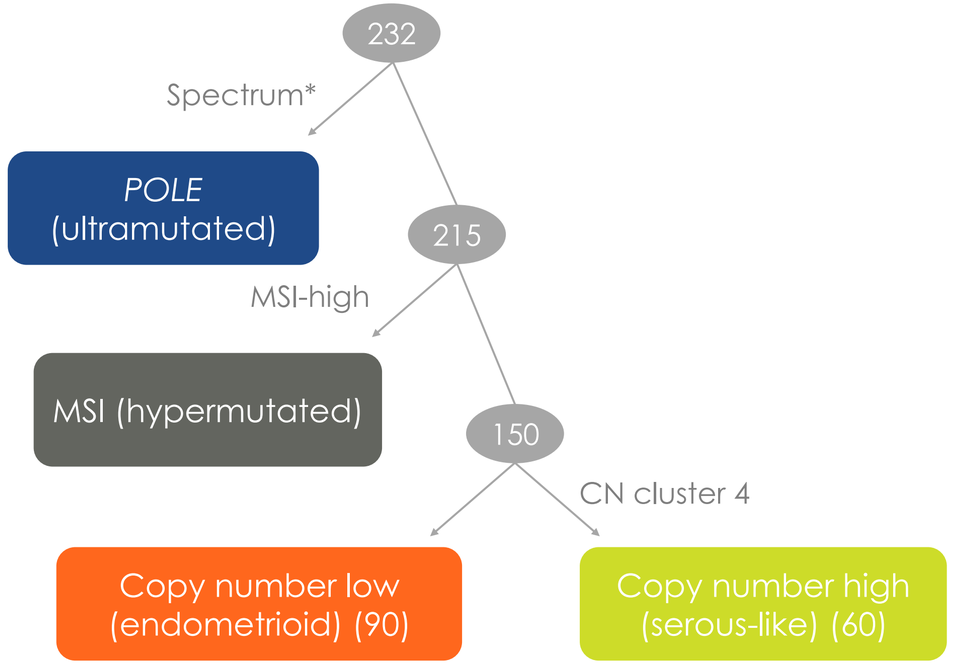


NSMP



TP53abn

Images provided by Dr. Concin.



Adapted from Cancer Genome Atlas Research Network. *Nature*. 2013;497:67-73.

*(%[CA] >0.2) AND (%[CG] >0.03) AND (SNV count >500)
CN = copy number; CNH = copy number–high; CNL = copy number–low; dMMR = mismatch repair deficient; IHC = immunohistochemistry; MSI = microsatellite instability; NSMP = nonspecific molecular profile; p53abn = p53 abnormal; p53mut = p53 mutation; POLEmut = polymerase ε-mutated; SNV = single-nucleotide variant.
1. Cancer Genome Atlas Research Network, et al. *Nature.* 2013;497:67-73. 2. Arciuolo DT, et al. *Int J Mol Sci.* 2022;23:11684.

Molecular Profiling in Endometrial Cancer

Therapeutic

- HER-2/*neu*
- MSI/MMR

Therapeutic and Prognos

- TP53
- Tumor mutational burden
  - POLE

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2024
Endometrial Carcinoma

NCCN Guidelines Index
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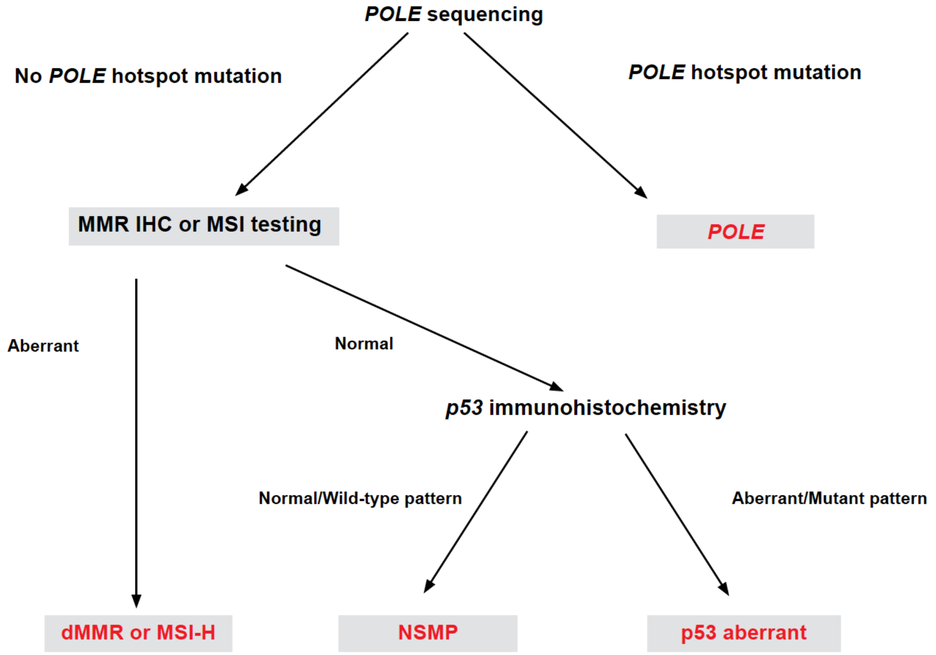
Discussion

PRINCIPLES OF MOLECULAR ANALYSIS

FIGURE 1: PATHOLOGY AND GENOMICS IN ENDOMETRIAL CARCINOMA
(The decision to use molecular testing/classification depends on the availability of resources and the multidisciplinary team of each center.)[f,g]



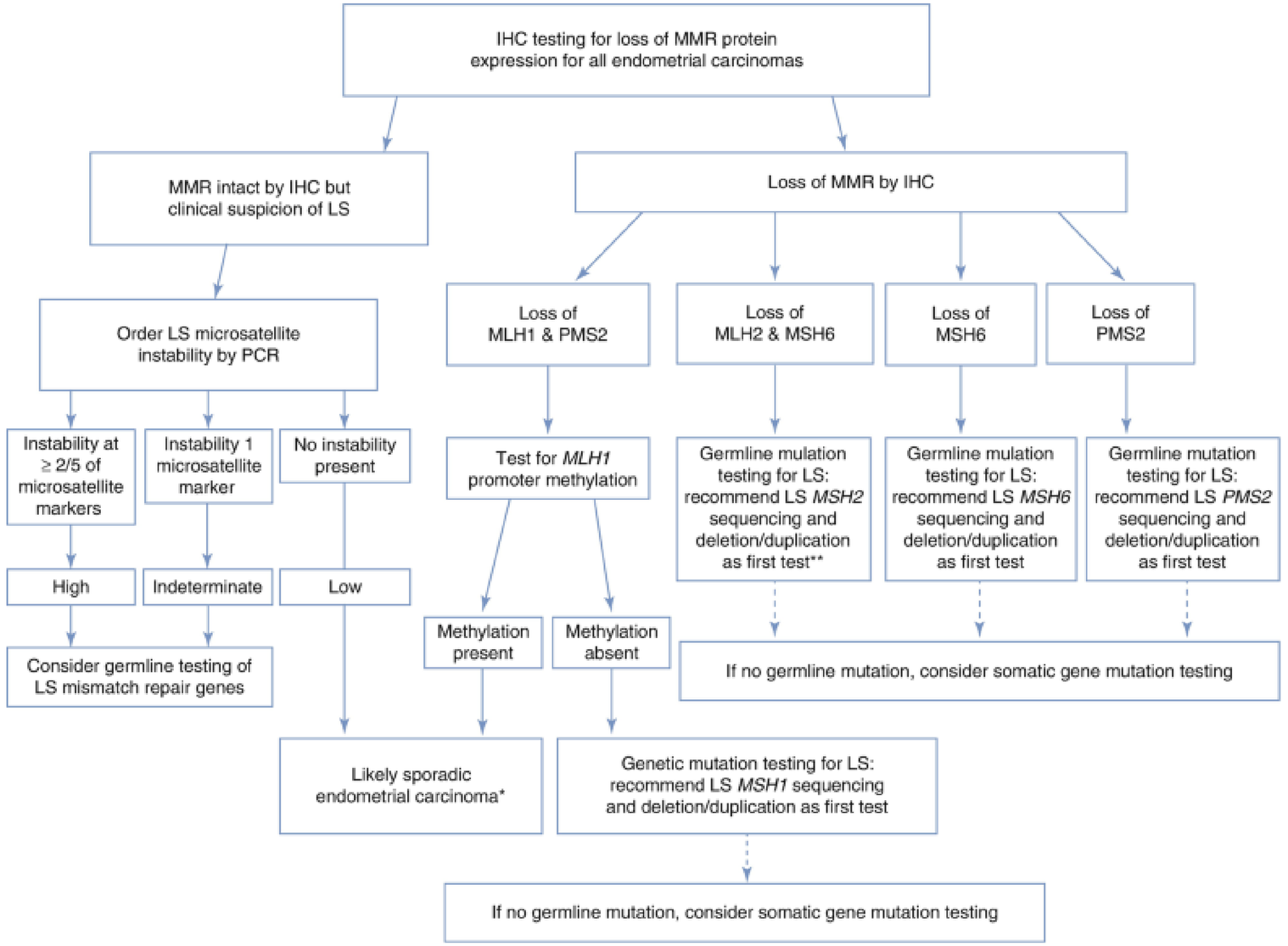
[f] Adapted with permission from Murali R, Delair DF, Bean SM, et al. Evolving roles of histologic evaluation and molecular/genomic profiling in the management of endometrial cancer. J Nat Compr Canc Netw 2018;16:201-209.
[g] Diagnostic algorithm for integrated genomic-pathologic classification of endometrial carcinomas.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

References

https://www.nccn.org/professionals/physician_gls/default.aspx

Molecular Profiling in Endometrial Cancer



* If strong clinical suspicion for LS, consider *MLH1* promoter methylation analysis of non-neoplastic tissue/peripheral blood to evaluate for germline epigenetic *MLH1* promoter methylation .
** If *MSH2* and *MSH6* unmutated, consider LS *EPCAM* sequencing and deletion/duplication.

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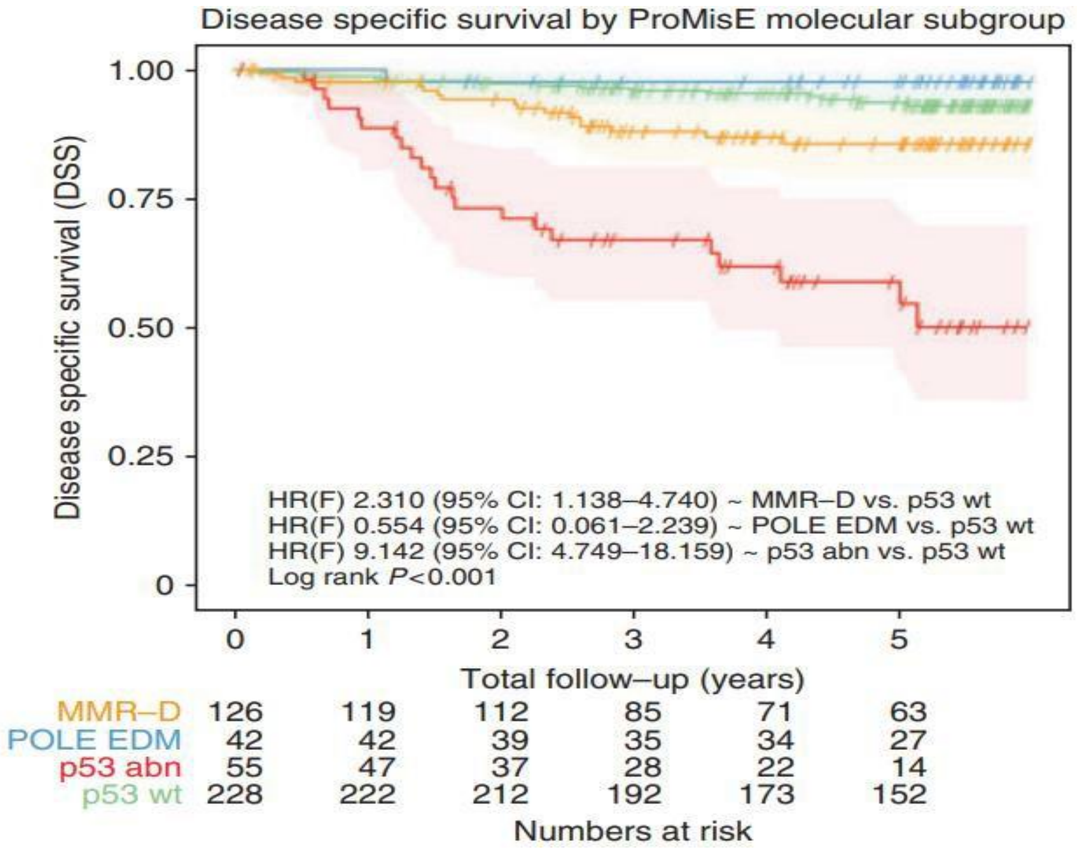
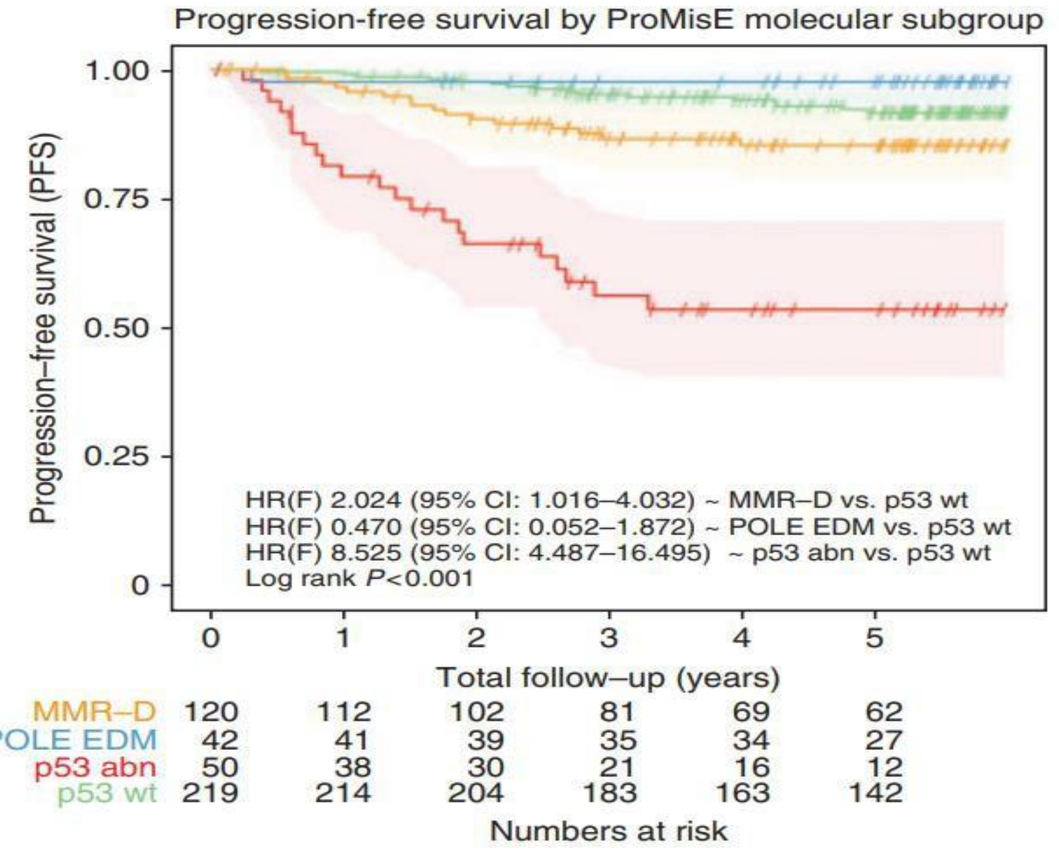
Proactive Molecular Risk Classifier for Endometrial Cancer ProMisE molecular subtypes





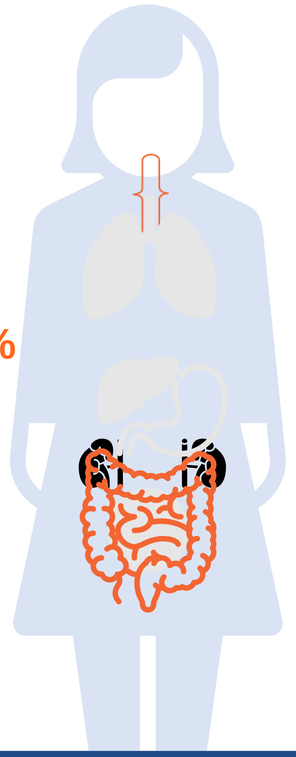
Source: Kommoss et al. Annals of Oncology 2018; 29: 1180–1188

dMMR/MSI-H Cancers are Found Throughout the Body

dMMR, mismatch repair deficient; MSI-H, microsatellite instability-high.

1. Zhao P, et al. *J Hematol Oncol*. 2019;12(1):54.
2. Lorenzi M, et al. *J Oncol.* 2020;2020:Article ID 1807929.

- Cancer types with the highest prevalence are **Lynch-syndrome-associated tumor types**[1]
- Non-lynch syndrome tumor types may also be affected[1]



Stomach: 9%–19.1%
Liver: 1%–3%

Endometrial: 17%–31.4%
Uterine: 3%–3.5%
Cervical: 2.6%–4%
Ovarian: 1.4%–2%

Esophageal: 1.6%
Mesothelioma: 2.4%

Adrenocortical: 4%

Colon: 6%–19.7%
Rectal: 6%

Not shown
Wilms tumor: 2.4%
Cholangiocarcinoma: 1.4%–3%

A meta-analysis of the prevalence of MSI-H/dMMR among tumor types with at least 5 publications showed that **endometrial cancer had the highest pooled MSI-H and dMMR prevalence (26% and 25% all stages, respectively)**[2]

- dMMR, mismatch repair deficient; MSI-H, microsatellite instability-high.
- 1. Zhao P, et al. *J Hematol Oncol*. 2019;12(1):54. 2. Lorenzi M, et al. *J Oncol.* 2020;2020:Article ID 1807929.

Measuring MSI/dMMR Can be Confusing

IHC test for 4 proteins

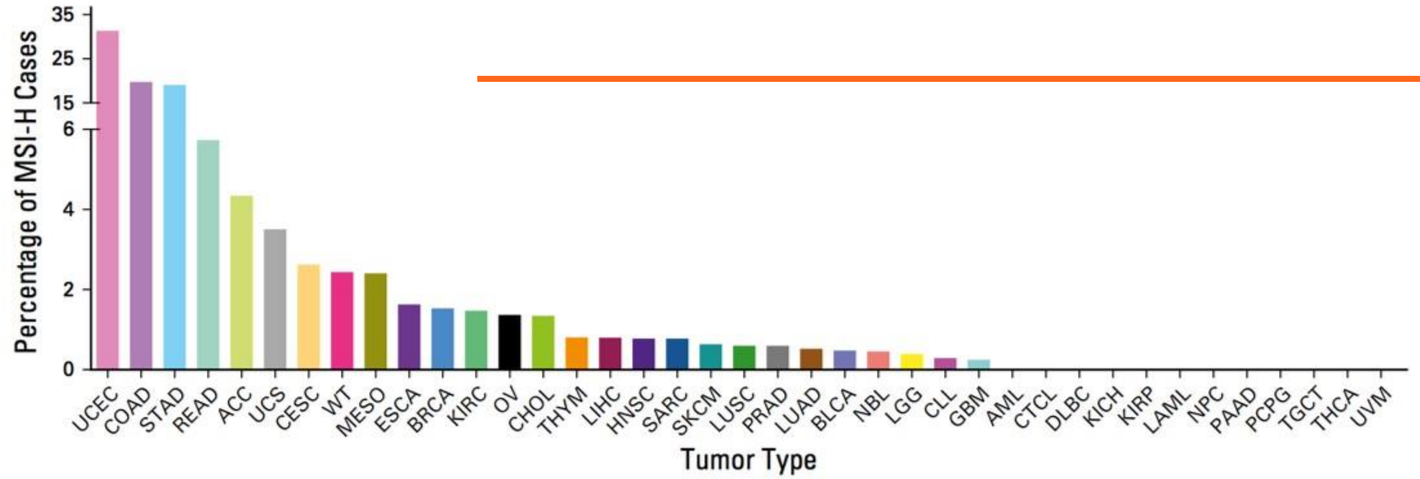
- MLH1, MSH6, PMS2, MSH2
- Present = normal
- Missing = consider reflex to gene test

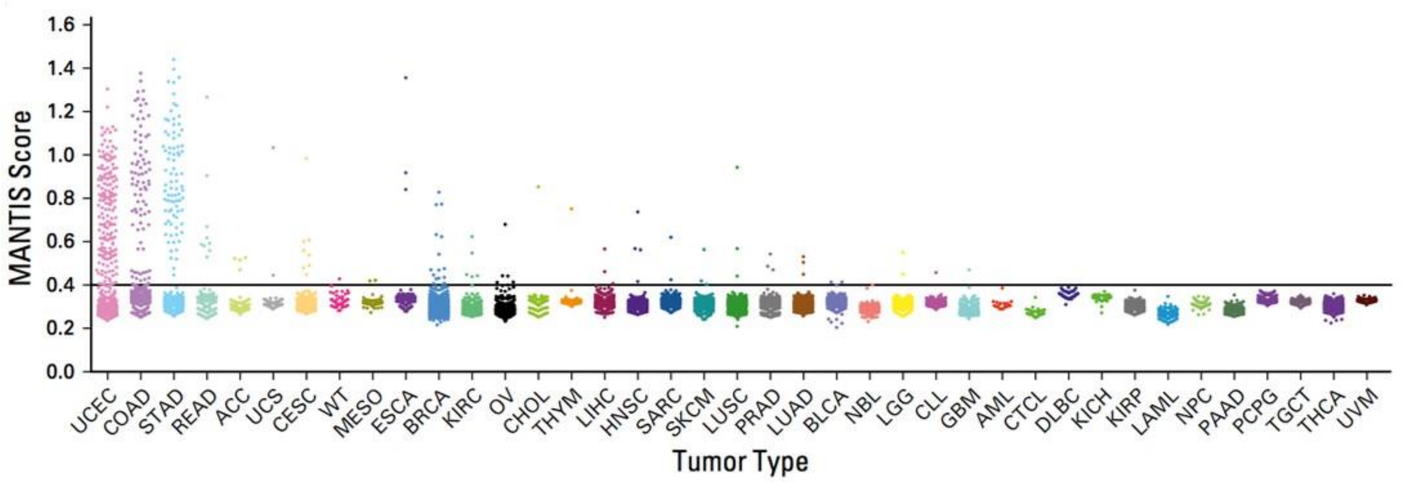
Gene sequencing

- Length of microsatellites compared with normal
- Can be done using next-generation sequencing platforms
- Need normal tissue

Germline vs somatic

MSI-H/dMMR in 39 Cancer Types; 11,139 Tumors





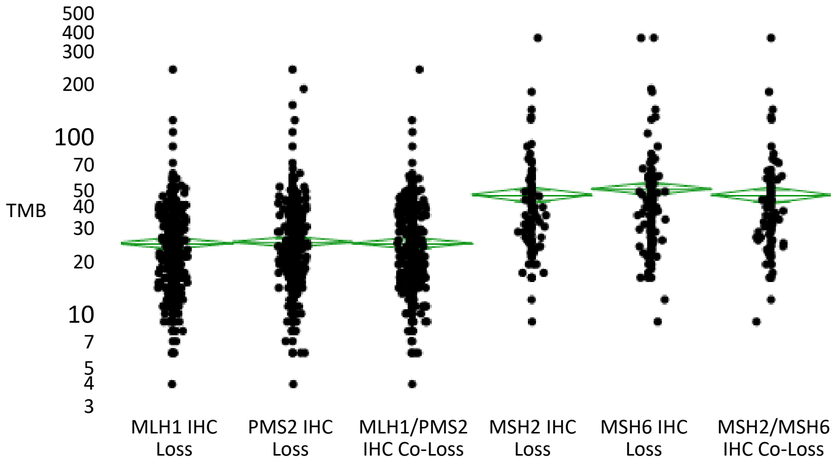
TOP 15

Uterine corpus endometrial carcinoma
Colon adenocarcinoma
Stomach adenocarcinoma
Rectal adenocarcinoma
Adrenocortical carcinoma
Uterine carcinosarcoma
Cervical squamous cell carcinoma and endocervical adenocarcinoma
Wilms tumor
Mesothelioma
Esophageal carcinoma
Breast carcinoma
Renal, clear cell
Ovarian serous cystadenocarcinoma
Cholangiocarcinoma
Thymoma

Bonneville. JCO Precis Oncol. 2017;2017.

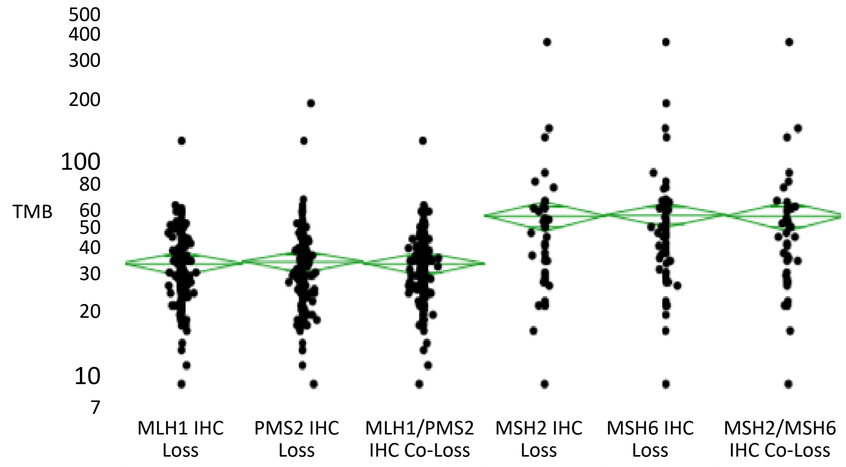
MSI-H Tumors Are Not Created Equal: Loss of MSH2/6 Associated With Higher TMB vs Loss of MLH1/PMS2

All Tumors



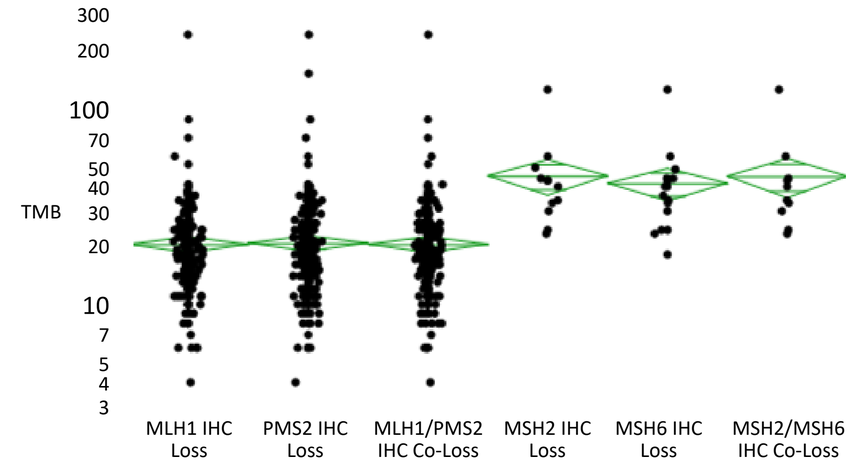
Mean mut/Mb	25	25	25	47	51	47

CRC



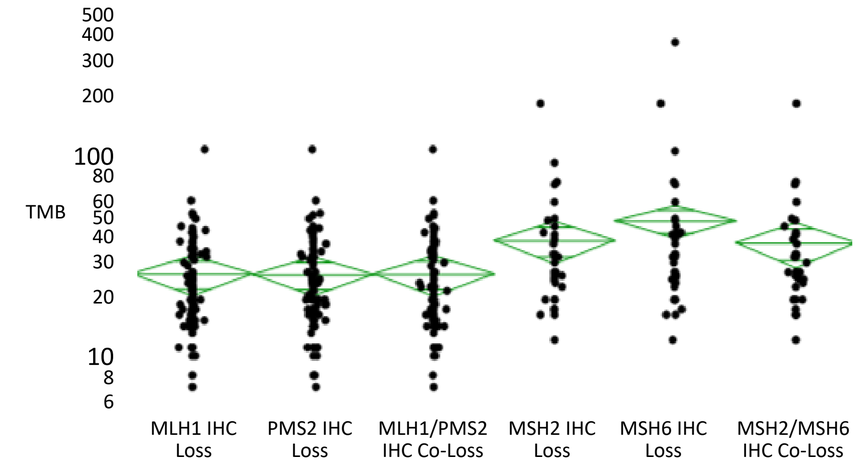
Mean mut/Mb	33	34	33	55	56	55

Endometrial



Mean mut/Mb	20	21	20	46	42	45

Other Cancers

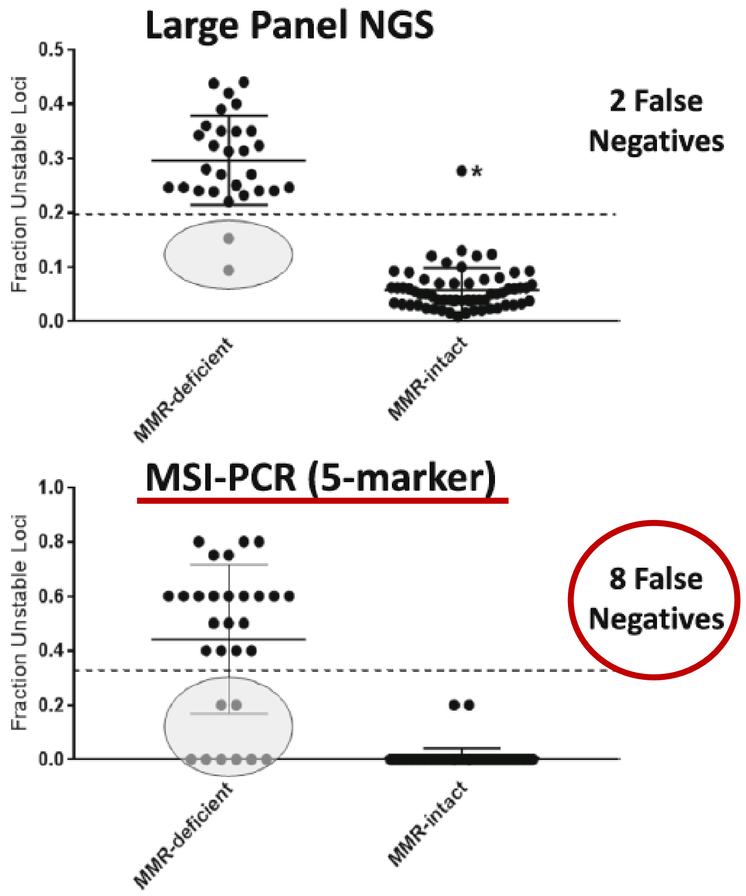


Mean mut/Mb	26	25	26	38	47	37

Hall. ASCO GI 2019. Abstr 505.

dMMR Testing: Methods

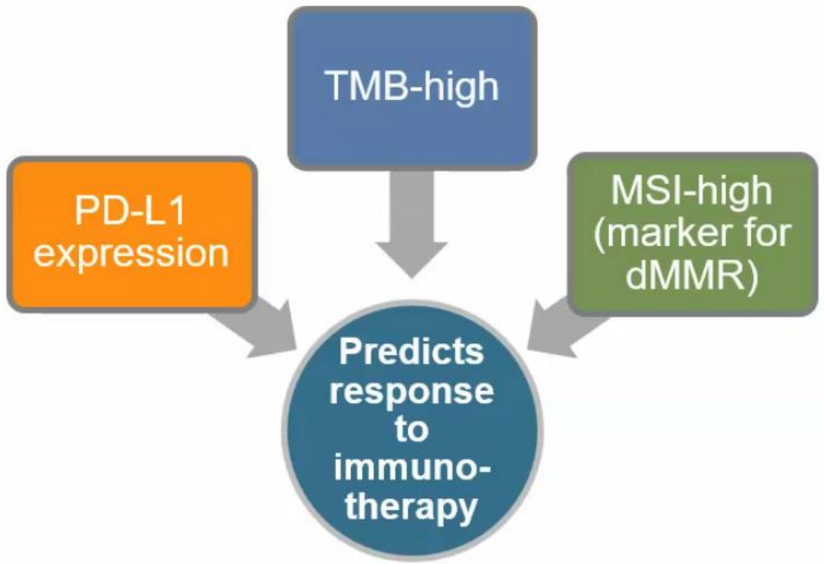
Test	Sensitivity	Specificity	Notes
MSI-PCR	97.0%	95.0%	5 marker loci; based on specific disease type Less accurate in noncolon; human interpretation; high DNA requirement
IHC (staining MMR protein)	92.0%	99.0%	Cannot detect loss of function mutations that do not affect the antigenicity of the targeted protein; human interpretation
CARIS MI	95.8%	99.4%	≥ 43 altered microsatellite loci
Foundation One	95.0%	98.0%	114 microsatellite loci
MANTIS	95.4%	98.9%	
MSISensor	95.4%	95.5%	



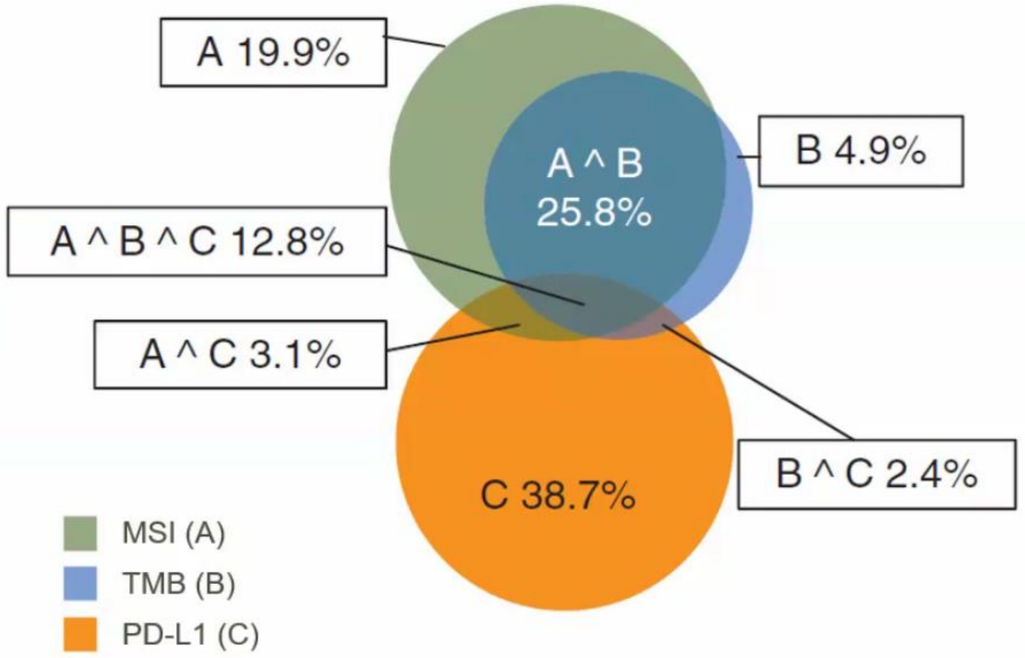
Hempelmann. J Immunother Cancer. 2018;6:29. Kautto. Oncotarget. 2017; 8:7452. Niu. Bioinformatics. 2014;30:1015.

Relationship between PD-L1, TMB and MSI in Endometrial Cancer

Overlap between PD-L1 expression, TMB-high, and MSI-high varies across tumor types[1,2]

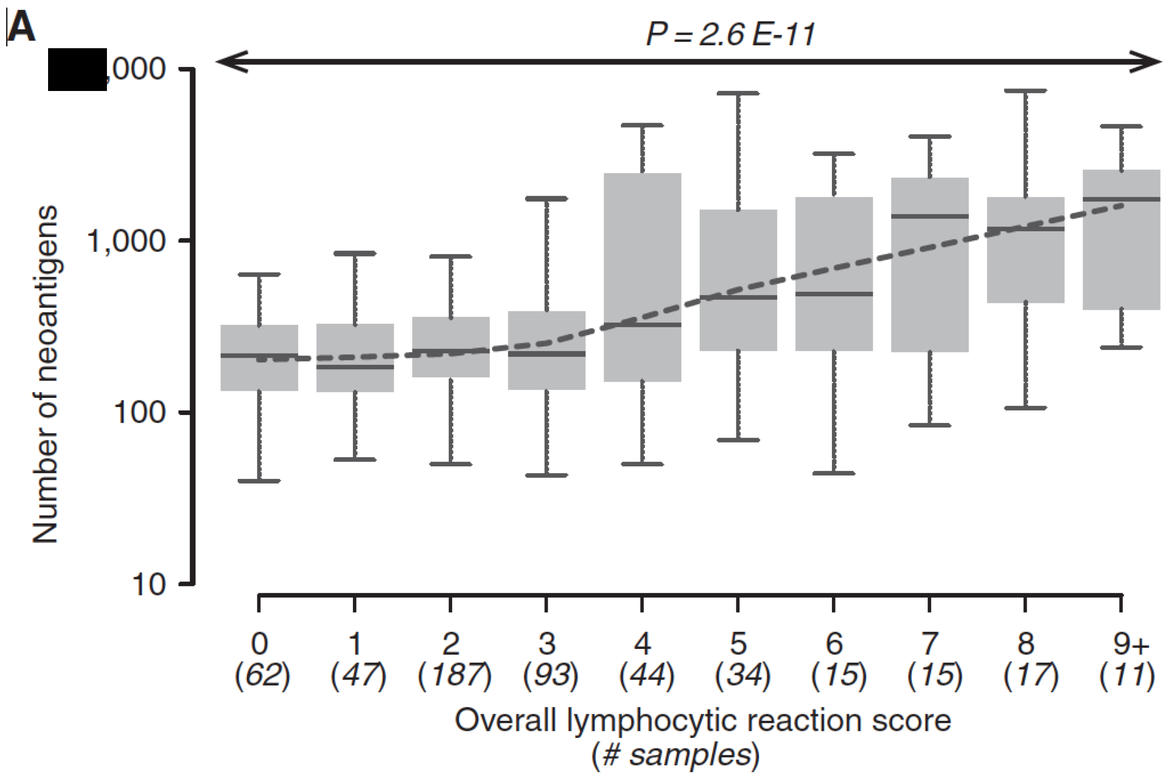


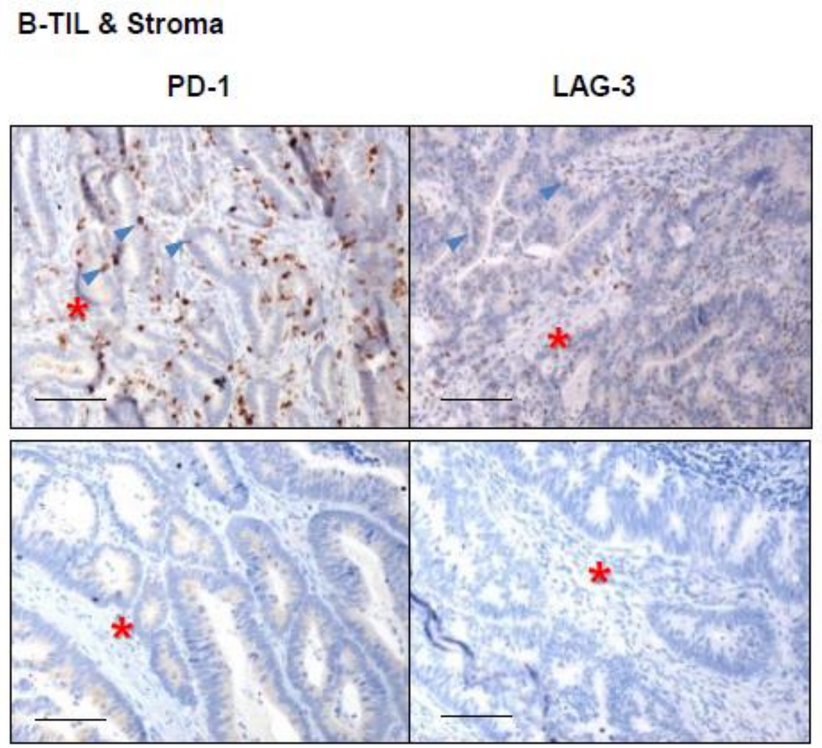
Relationship between MSI, TMB, and PD-L1 expression in EC*[1]



*Out of 4186 cases (100%) of solid tumors and generic cancer types.[1]
MMR, mismatch repair; MSI, microsatellite instability; PD-L1, programmed cell death ligand 1; TMB, tumor mutational burden.
1. Luchini C et al. *Ann Oncol.* 2019;30:1232-1243. **2.** Vanderwalde A et al. *Cancer Med.* 2018;7(3):746-756.

Cancers Associated with MSI Have Greater T-Cell Infiltrate and Checkpoint Expression





1. Giannakis. Cell Rep. 2016;15:857. 2. Llosa. Cancer Discov. 2015;5:43.

FIGO Staging of Endometrial Cancer: 2023

- Data and analyses from the molecular and histological classifications performed and published in the recently developed ESGO/ESTRO/ESP guidelines were used as a template for adding the new subclassifications to the proposed molecular and histological staging system.

- Grade of the lesion, the histological type and LVSI must be recorded. If available and feasible, molecular classification testing (POLEmut, MMRd, NSMP, p53abn) is encouraged in all patients with endometrial cancer for prognostic risk-group stratification and as factors that might influence adjuvant and systemic treatment decisions

Berek JS et al. J Gynecol Oncol. 2023 Sep;34(5):e85.

FIGO Staging of Endometrial Cancer: 2023

Stage	Description
Stage I	Confined to the uterine corpus and ovary[c]
IA	Disease limited to the endometrium OR non-aggressive histological type, i.e. low-grade endometroid, with invasion of less than half of myometrium with no or focal lymphovascular space involvement (LVSI) OR good prognosis disease
	IA1 Non-aggressive histological type limited to an endometrial polyp OR confined to the endometrium
	IA2 Non-aggressive histological types involving less than half of the myometrium with no or focal LVSI
	IA3 Low-grade endometrioid carcinomas limited to the uterus and ovary[c]
IB	Non-aggressive histological types with invasion of half or more of the myometrium, and with no or focal LVSI[d]
IC	Aggressive histological types[e] limited to a polyp or confined to the endometrium
Stage II	Invasion of cervical stroma with extrauterine extension OR with substantial LVSI OR aggressive histological types with myometrial invasion
IIA	Invasion of the cervical stroma of non-aggressive histological types
IIB	Substantial LVSI[d] of non-aggressive histological types
IIC	Aggressive histological types[e] with any myometrial involvement
Stage III	Local and/or regional spread of the tumor of any histological subtype
IIIA	Invasion of uterine serosa, adnexa, or both by direct extension or metastasis
	IIIA1 Spread to ovary or fallopian tube (except when meeting stage IA3 criteria)[c] IIIA2 Involvement of uterine subserosa or spread through the uterine serosa
IIIB	Metastasis or direct spread to the vagina and/or to the parametria or pelvic peritoneum
	IIIB1 Metastasis or direct spread to the vagina and/or the parametria IIIB2 Metastasis to the pelvic peritoneum
IIIC	Metastasis to the pelvic or para-aortic lymph nodes or both[f]
	IIIC1 Metastasis to the pelvic lymph nodes IIIC1i Micrometastasis IIICii Macrometastasis IIIC2 Metastasis to para-aortic lymph nodes up to the renal vessels, with or without metastasis to the pelvic lymph nodes IIIC2i Micrometastasis IIIC2ii Macrometastasis
Stage IV	Spread to the bladder mucosa and/or intestinal mucosa and/or distance metastasis
IVA	Invasion of the bladder mucosa and/or the intestinal/bowel mucosa
IVB	Abdominal peritoneal metastasis beyond the pelvis
IVC	Distant metastasis, including metastasis to any extra- or intra-abdominal lymph nodes above the renal vessels, lungs, liver, brain, or bone

Berek JS et al. J Gynecol Oncol. 2023 Sep;34(5):e85.

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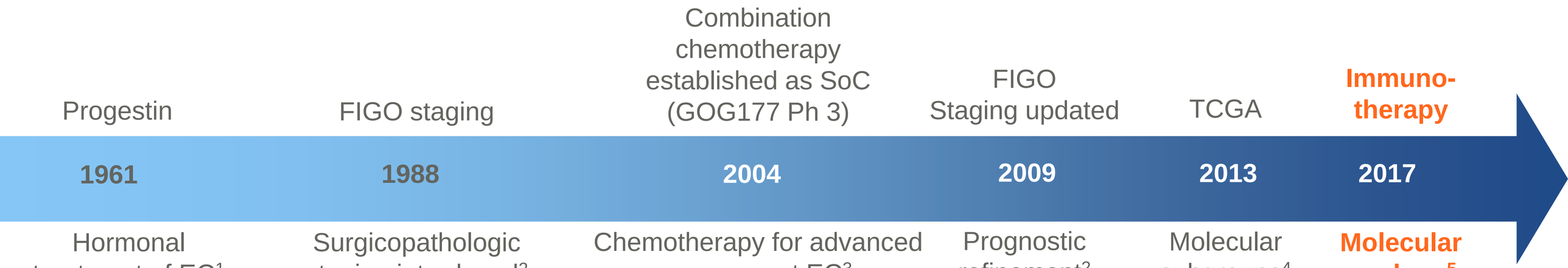
Immunotherapy Based On Molecular Characterization Is the Most Recent Therapeutic Breakthrough in EC Treatment



ESGO/ESTRO/ESP guidelines recommend molecular classification in all endometrial cancers, and considering pembrolizumab for second-line treatment of dMMR/MSI carcinomas[5]

NCCN Clinical Practice Guidelines In Oncology (NCCN Guidelines®) recommend molecular analysis of endometrial cancers, including universal testing for MMR/MSI, and considering pembrolizumab,[a] nivolumab,[b] or dostarlimab[c] for second-line treatment of dMMR/MSI-H tumors[6]

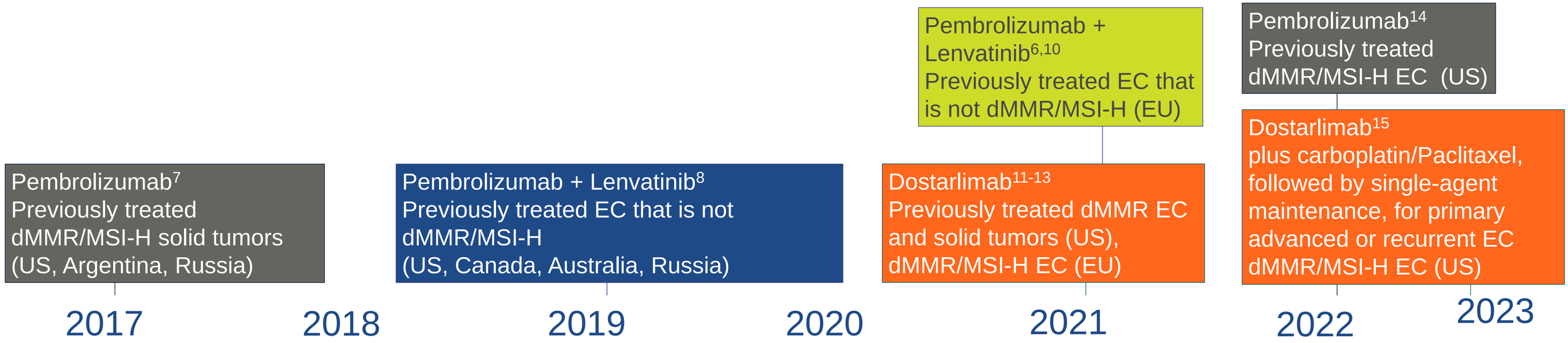
[a]For recurrent endometrial cancer, NCCN recommends MSI-H or dMMR testing if not previously done. Pembrolizumab is indicated for patients with MSI-H or dMMR tumors that have progressed following prior treatment. [b]For dMMR recurrent, metastatic, or high-risk endometrial carcinoma. [c]Dostarlimab-gxly is indicated for patients with dMMR recurrent or advanced EC that has progressed on or following prior treatment with a platinum-containing regimen.

dMMR, mismatch repair deficient; EC, endometrial cancer; FIGO, International Federation of Gynecologists and Obstetricians; GOG, Gynecologic Oncology Group; MMR, mismatch repair; MSI, microsatellite instability; MSI-H, microsatellite instability-high; NCCN, National Comprehensive Cancer Network®; SoC, Standard of Care.

1. Yang S, et al. *Discov Med*. 2011;12:205-12. 2. Haltia U-M, et al. *J Gynecol Oncol*. 2014;25:30-35. 3. Fleming GF, et al. *J Clin Oncol.* 2004;22:2159-2166. 4. Cancer Genome Atlas Research Network, et al. *Nature*. 2013;497:67-73. 5. Concin N, et al. *Int J Gynecol Cancer.* 2021;31:12-39. 6. National Comprehensive Cancer Network (NCCN)® Clinical Practice Guidelines in Oncology. Uterine Neoplasms, Version 3.2021. Accessed July 22, 2021.

Evolving Treatment Landscape for Advanced/Recurrent or High-risk Endometrial Carcinoma

- Historically treatment guidelines recommend platinum-based chemotherapy (carboplatin + paclitaxel) as preferred 1L treatment of advanced/recurrent EC[1,2,a]
- In 2L treatment, guidelines recommend PD-1 regimens based on biomarker (MMR/MSI) status[2]
- Guideline recommendations are based on recent approvals of PD-1 agents in previously treated EC[3-5,6]



[a]Hormone therapy is included as a preferred 1L therapy In low grade carcinomas without rapidly progressive disease. 1L, first line; 2L, second line; CRC, colorectal cancer; dMMR, mismatch repair deficient; EC, endometrial cancer; EU, European Union; MMR, mismatch repair; MSI, microsatellite instability; MSI-H, microsatellite instability-high; PD-1, programmed death 1; US, United States.

1. Colombo N et al. *Ann Oncol*. 2016;27:16–41. 2. Concin N et al. *Int J Gynecol Cancer*. 2021;31:13–39. 3. Keytruda [prescribing information]. Whitehouse Station. NJ: Merck Sharp & Dohme Corp.; 2021. 4. Jemperli (dostarlimab-gxly) injection, for intravenous use [prescribing information]. Research Triangle Park, NC, USA: GlaxoSmithKline LLC; 2021. 5. Jemperli (Dostarlimab 500 mg solution for infusion) [Summary of product characteristics]. Dublin, Ireland: GlaxoSmithKline (Ireland) Limited; 2021. 6. Keytruda (pembrolizumab) [Summary of product characteristics]. Merck Sharp & Dohme B.V. Netherlands: 2021. 7. US FDA. Press Release. Available at: https://www.fda.gov/news-events/press-announcements/fda-approves-first-cancer-treatment-any-solid-tumor-specific-genetic-feature. Accessed May 14, 2021. 8. US FDA. Press Release. Available at: https://www.fda.gov/drugs/resources-information-approved-drugs/simultaneous-review-decisions-pembrolizumab-plus-lenvatinib-australia-canada-and-us. Accessed May 14, 2021. 9. US FDA. Press Release. Available at: https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-pembrolizumab-first-line-treatment-msi-hdmmr-colorectal-cancer. Accessed December 13, 2021. 10. Merck. Press Release. Available at: https://www.merck.com/news/european-commission-approves-keytruda-pembrolizumab-plus-lenvima-lenvatinib-for-patients-with-certain-types-of-endometrial-carcinoma/ Accessed: March 29, 2022.11. FDA Approves Immunotherapy for Endometrial Cancer with Specific Biomarker | FDA. | FDA Accessed June 7, 2021. 12. EMA: Jemperli. Available at: https://www.ema.europa.eu/en/medicines/human/EPAR/jemperli. Accessed June 7, 2021. 13. US FDA. Press Release. Available at: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-dostarlimab-gxly-dmmr-advanced-solid-tumors. Accessed September 22, 2021. 14. US FDA Press Release. Available at: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-pembrolizumab-advanced-endometrial-carcinoma. Accessed March 28, 2022. 15. https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-dostarlimab-gxly-chemotherapy-endometrial-cancer

Clinical Data of Single Agent Immunotherapy in 2L Endometrial Cancer

Pembrolizumab (KN-158): Robust Antitumor Activity in Patients With MSI-H Advanced EC

Variable	MSI-H EC n = 79	EC (biomarker unselected) n = 107
ORR % (95% CI)	**48** (37-60)	**11.2** (5.9-18.8)
Complete response	11 (14)	0
Partial response	27 (34)	12 (11.2)
Stable disease	14 (18)	26 (24.3)
Progressive disease	23 (29)	56 (52.3)
Not evaluable	1 (1)	2 (1.9)
Not assessed	3 (4)	11 (10.3)

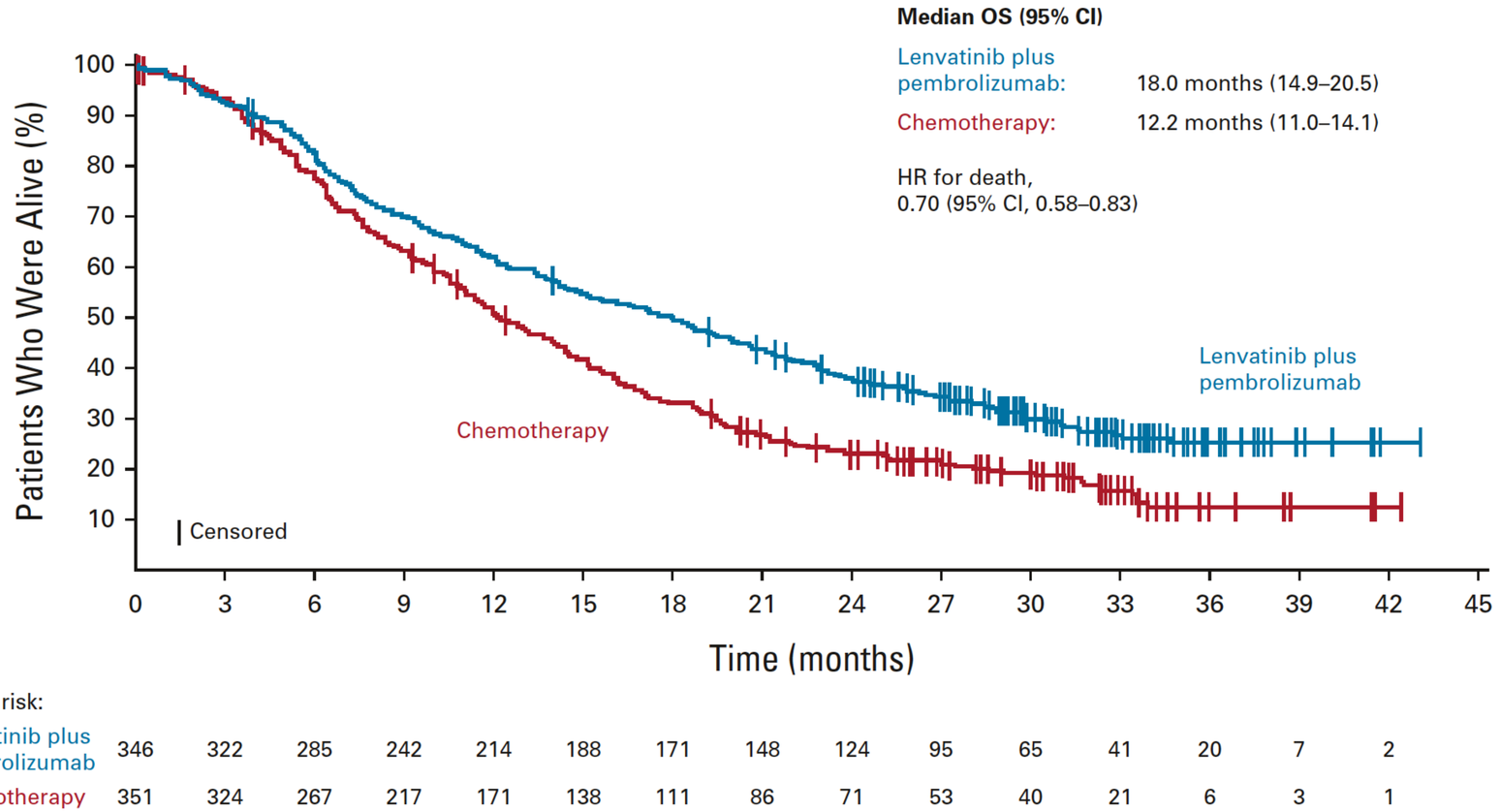
O'Malley DM et al. J Clin Oncol. 2022 Mar 1;40(7):752-761.

Dostarlimab (GARNET Cohorts A1 & A2): Clinical Benefit in dMMR and MMRp EC Patients

Variable	dMMR EC n = 103	MMRp EC n = 142
ORR % (95% CI)	**46** (34.9-54.8)	**19** (8.3-20.1)
Complete response	11 (10.7)	3 (2.1)
Partial response	35 (34.0)	16 (11.3)
Stable disease	13 (12.6)	31 (21.8)
Progressive disease	39 (37.9)	77 (54.2)
Not evaluable	3 (2.9)	0
Not done	2 (1.9)	15 (10.6)

Oaknin A et al. J Immunother Cancer. 2022 Jan;10(1):e003777.

Lenvatinib Plus Pembrolizumab in Previously Treated Advanced Endometrial Cancer: Updated Efficacy and Safety From the Randomized Phase III Study 309/KEYNOTE-775



ORR in pMMR patients: 32.4% *v* 15.1%

Median follow-up was 18.7 months in the lenvatinib plus pembrolizumab arm and 12.2 months in the chemotherapy arm (14.7 months overall)

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Makker V, Colombo N, Herráez AC, Monk BJ, Mackay H, Santin AD, Miller DS, Moore RG, Baron-Hay S, Ray-Coquard I, Ushijima K, Yonemori K, Kim YM, Guerra Alia EM, Sanli UA, Bird S, Orlowski R, McKenzie J, Okpara C, Barresi G, Lorusso D.
J Clin Oncol. 2023 Jun 1;41(16):2904-2910.

Redefining the Position of Hormonal Therapy in Endometrial Cancer in the Era of Molecular Classification

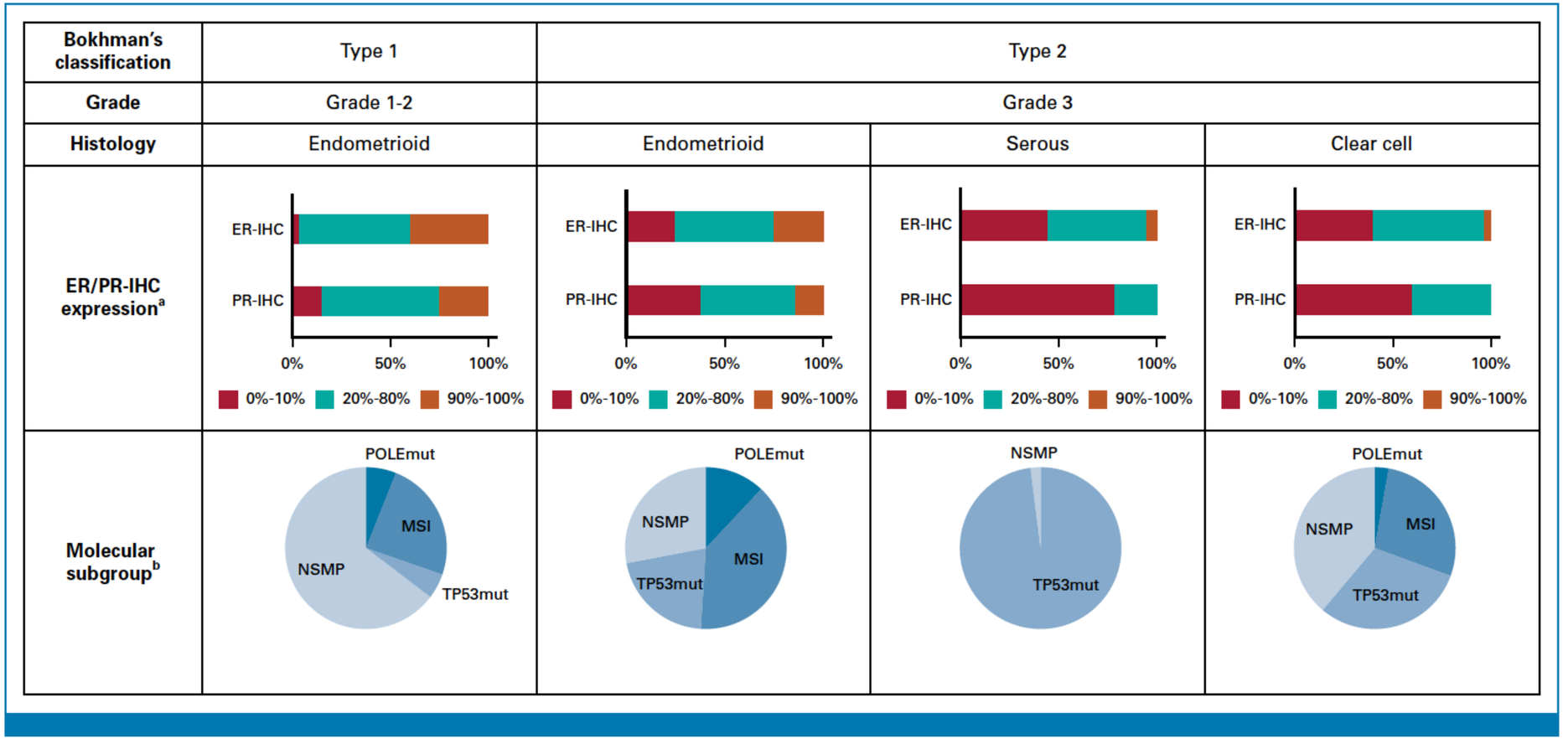

FIG 1. Relation between type 1 and type 2 endometrial cancers, immunohistochemical expression of ER-IHC/PR-IHC in relation to tumor grade, and molecular classification. [a]On the basis of data from van Weelden et al. [b]Data from Travaglino et al,[6] Urick et al,[9] and Reijnen et al.[7] ER, estrogen receptor; IHC, immunohistochemistry; MSI, microsatellite instability; NSMP, no specific molecular profile[5-7]; POLEmut, polymerase epsilon–mutated; PR, progesterone receptor; TP53mut, tumor protein p53-mutated.

Pijnenborg JMA et. al. J Clin Oncol. 2023 Oct 3:JCO2300470. doi: 10.1200/JCO.23.00470. Online ahead of print.

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