Table 2. Overview of studies on prevalences of overall MMRd, MMRd based on *MLH1* promoter methylation (*MLH1*-PM), germline or somatic (likely) pathogenic variants (PV) or unexplained MMRd (UMMRd) across different cancer types.

Study characteristics		Prevalence					Age and Sex
Author (year)	Study design	Overall MMRd (IHC MMR) or MSI	Loss of *MLH1*/*PMS2*, *MLH1*-PM	Germline (likely) PV MMR gene	Somatic (likely) PV MMR gene and/or LOH	UMMRd	
Epithelial ovarian cancer (EOC)							
Mitric (2023)	Meta-analysis	<u>EOC overall</u> • MMRd: 6% (95% CI 5% to 8%), I^2 of 80%, based on N=328/5814 patients from 27 studies • MSI-H: 13% (95% CI 12% to 15%), I^2 of 0%, based on N=315/2375 patients from 14 studies <u>Endometrioid</u> • MMRd: 12% (95% CI 9% to 16%), I^2 of 60%, based on N=193/1625 patients from 19 studies • MSI-H: 12% (95% CI 8% to 18%), I^2 of 0%, based on N=19/158 patients from 5 studies <u>Serous</u> • MMRd: 1% (95% CI 0% to 2%), I^2 of 56%, based on N=16/1903 patients from 12 studies	• *MLH1*-PM: 76% (95% CI 64% to 84%), I^2 of 0%, based on N=53/70 patients with *MLH1* deficiency from 13 studies	<u>EOC overall</u> • 2% (95% CI 1% to 3%), I^2 of 88%, based on N=232/14809 patients from 14 studies <u>Endometrioid</u> • 3% (95% CI 2% to 5%), I^2 of 58%, based on N=42/1198 patients from 6 studies <u>Serous</u> • 1% (95% CI 0% to 2%), I^2 of 84%, based on N=43/6016 patients from 7 studies <u>Other</u> • 1% (95% CI 0% to 2%), I^2 of 0%, based on N=11/1043 patients from 6 studies	Not reported	Not reported	• Information about age at diagnosis not reported • 100% female

Bijlage: Table 2. Overview of studies on prevalences of overall MMRd, MMRd based on *MLH1* promoter methylation (*MLH1*-PM), germline or somatic (likely) pathogenic variants (PV) or unexplained MMRd (UMMRd) across different cancer types.

Study characteristics		Prevalence					Age and Sex
Author (year)	Study design	Overall MMRd (IHC MMR) or MSI	Loss of *MLH1*/*PMS2*, *MLH1*-PM	Germline (likely) PV MMR gene	Somatic (likely) PV MMR gene and/or LOH	UMMRd	
		• MSI-H: 9% (95% CI 4% to 19%), I^2 of 0%, based on N=71/556 patients from 6 studies <u>Other</u> • MMRd: 3% (95% CI 1% to 14%), I^2 of 0%, based on N=24/465 patients from 14 studies • MSI-H: 13% (95% CI 8% to 20%), I^2 of 0%, based on N=16/125 patients from 5 studies					
Summary *Range or estimate upon availability*		• MMRd: 1% (serous) - 12% (endometrioid) • MSI-H: 9% (serous) - 13% (other) *Source: Mitric (2023)*	• *MLH1*-PM: 76% (95% CI 64% to 84%) based on patients with lost *MLH1* *Source: Mitric (2023)*	• 1% (95% CI 0% to 2%) *Source: Mitric (2023)*	Not reported	Not reported	Not reported
Pancreatic ductal cancer (PDAC), biliary tract cancer (BTC) and gallbladder cancer (GBC)							
Agaram (2010) • Ampullary adenocarcinomas	Retrospective cohort study • Setting: Pathology database of MSKCC, New York • Period: not reported	• MMRd: N=3/54 (5.6%)	• Lost *MLH1*/*PMS2*: N=1/3 (33.3%) MMRd patients	Not reported	Not reported	Not reported	<u>Total cohort</u> • Mean age of 64y • N=20/54 (37.0%) females

Bijlage: Table 2. Overview of studies on prevalences of overall MMRd, MMRd based on *MLH1* promoter methylation (*MLH1*-PM), germline or somatic (likely) pathogenic variants (PV) or unexplained MMRd (UMMRd) across different cancer types.

Study characteristics		Prevalence					Age and Sex
Author (year)	Study design	Overall MMRd (IHC MMR) or MSI	Loss of *MLH1*/*PMS2*, *MLH1*-PM	Germline (likely) PV MMR gene	Somatic (likely) PV MMR gene and/or LOH	UMMRd	
Hu (2018) • Pancreatic adenocarcinoma	Retrospective cohort study • Setting: MSKCC institutional tumor registry • Period: 2006-2017	• MMRd by IHC, germline testing or NGS: N=7/833 (0.8%)	• Not reported	• N=7/7 (100%) MMRd patients • Overall: N=7/833 (0.8%)	Not reported	Not reported	MMRd tumours • Age range: 42-88y • Sex not reported
Christakis (2019) • Upper gastrointestinal tract carcinomas	Institutional cohort study • Setting: Dana Farber Cancer Institute, Boston, USA • Period: not reported	Pancreas • MSI: N=2/199 (1.0%) Gallbladder • MSI: N=0/19 (0%) Bile duct • MSI: N=1/60 (2%) Ampullary • MSI: N=0/11 (0%)	Pancreas • Lost *MLH1*/*PMS2*: N=1/2 (50%) MSI patients→ data on *MLH1*PM not reported Gallbladder • Not reported Bile duct • Not available Ampullary • Not reported	Pancreas • Overall: N=1/199 (0.5%) Gallbladder • Not reported Bile duct • Not reported Ampullary • Not reported	Pancreas • 1/199 (0.5%) Gallbladder • Not reported Bile duct • Not available Ampullary • Not reported	Pancreas • Not reported Gallbladder • Not reported Bile duct • Not reported Ampullary • Not reported	Total cohort • Median age: 65.3y (range, 19-93.6) • N=219/645 (34%) females LS patients • Median age: 69.6y (range, 49.8-74.6) • Sex not reported
Abrha (2020) • Gastrointestinal malignancies	Retrospective cohort study • Setting: SCCI • Period: January 2016 – December 2017	Pancreas • MMRd: N=13/244 (5.3%) → 3/13 MMRd cases were ampullary carcinomas Gallbladder • MMRd: N=1/41 (2.5%) Cholangiocarcinoma • MMRd: N=0/44 (0%) Ampullary • MMRd: N=3/14 (21.4%)	Pancreas • *MLH1*-PM: N=3/13 (23.1%) MMRd patients (n=5 false positives) Gallbladder • Not reported Cholangiocarcinoma • Not reported Ampullary • *MLH1*-PM: N=2/3 (66.7%) MMRd patients	Pancreas • N=3/13 (23.1%) MMRd patients (n=5 false positives) • Overall: N=3/244 (1.2%) Gallbladder • Not reported Cholangiocarcinoma • Not reported Ampullary • Not reported	Pancreas • Double somatic: N=2/13 (15.4%) MMRd patients (n=5 false positives) • Possibly double somatic: N=3/13 (23.1%) MMRd patients (n=5 false positives) Gallbladder • Not reported Cholangiocarcinoma	Pancreas • N=2/13 (11.1%) MMRd patients (n=5 false positives) Gallbladder • Not reported Cholangiocarcinoma • Not reported Ampullary • Not reported	Pancreatic MMRd patients • Median age at diagnosis: 66y (IQR, 57-72) • N=7/13 (54%) females Gallbladder • Not reported Cholangiocarcinoma • Not reported Ampullary • Not reported

Bijlage: Table 2. Overview of studies on prevalences of overall MMRd, MMRd based on *MLH1* promoter methylation (*MLH1*-PM), germline or somatic (likely) pathogenic variants (PV) or unexplained MMRd (UMMRd) across different cancer types.

Study characteristics		Prevalence					Age and Sex
Author (year)	Study design	Overall MMRd (IHC MMR) or MSI	Loss of *MLH1*/*PMS2*, *MLH1*-PM	Germline (likely) PV MMR gene	Somatic (likely) PV MMR gene and/or LOH	UMMRd	
					• Not reported <u>Ampullary</u> • Not reported		
Mettman (2020) • Pancreatic adenocarcinoma	Retrospective cohort study • Setting: Department of Pathology and Laboratory Medicine, University of Kansas Medical Center • Period: December 2017 – September 2019	• N=184 pancreatic fine-needle aspiration specimens • N=65/184 (35.3%) with sufficient material to perform IHC • IHC: N=5/65 (7.7%) absence of labeling for one or two of the MMR proteins, but results were invalid	Not reported	Not reported	Not reported	Not reported	<u>Cohort that underwent IHC MMR testing</u> • Median age: 71y (range, 34-93) • N=30/65 (64.2%) females
Grant (2021) • Pancreatic adenocarcinoma	Retrospective cohort study • Setting: Ontario Pancreas Study, Canada • Period: not reported	<u>Clinical cohort</u> • MMRd by IHC or WGS: N=12/1213 (1.0%), not all tested: MMRd by IHC: N=8/53 (7.5%) <u>Genomics cohort</u> • MSI-H by WGS: N=9/288 (3.1%)	<u>Genomics cohort</u> • Lost *MLH1*/*PMS2*: N=2/288 (0.7%) MMRd patients	• N=14/519 (2.7%) patients that underwent germline MMR gene sequencing	N=4/288 (1.4%) from the genomics cohort who had MMRd tumours	Not reported	<u>MMRd tumours</u> • Median age: 61.5y (IQR, 52.5-74.8) • N=8/12 (66.7%) females
Kryklyva (2022) • Ampullary and pancreatic carcinoma, early onset (<50y)	Retrospective cohort study • Setting: PALGA • Period: January 2002-December 2012	<u>Pancreas</u> • MSI: N=2/44 (4.5%) <u>Ampullary</u> • MSI: N=1/23 (4.3%)	<u>Pancreas</u> • Lost *MLH1*/*PMS2*: N=0/2 (0%) MSI patients <u>Ampullary</u>	<u>Pancreas</u> • N=2/2 (100%) MSI patients • Overall: N=2/44 (4.5%) <u>Ampullary</u>	<u>Pancreas</u> • N=0/2 (0%) MSI patients <u>Ampullary</u> • N=0/1 (0%) MSI patients	<u>Pancreas</u> • N=0/2 (0%) MSI patients <u>Ampullary</u> • N=0/1 (0%) MSI patients	<u>Pancreas</u> • Age: 43y (range, 30-49) • N=16/44 (36.4%) females <u>Ampullary</u>

Bijlage: Table 2. Overview of studies on prevalences of overall MMRd, MMRd based on *MLH1* promoter methylation (*MLH1*-PM), germline or somatic (likely) pathogenic variants (PV) or unexplained MMRd (UMMRd) across different cancer types.

Study characteristics		Prevalence					Age and Sex
Author (year)	Study design	Overall MMRd (IHC MMR) or MSI	Loss of *MLH1*/*PMS2*, *MLH1*-PM	Germline (likely) PV MMR gene	Somatic (likely) PV MMR gene and/or LOH	UMMRd	
			• Lost *MLH1*/*PMS2*: N=1/1 (100%) MSI patients	• N=1/1 (100%) MSI- patients • Overall: N=1/23 (4.3%)			• Age: 44y (range, 33-49) • N=13/23 (56.5%) females
Kubo (2022) • Hepato-biliary-pancreatic malignancies	Retrospective cohort study • Setting: 7 hospitals in the KHBO Group • Period: January 2019-April 2021	<u>Pancreas</u> • MSI-H: N=2/144 (1.4%) <u>Gallbladder</u> • MSI-H: N=1/18 (5.6%) <u>Cholangiocarcinoma</u> • MSI-H: N=8/88 (9.1%)	<u>Pancreas</u> • Not reported <u>Gallbladder</u> • Not reported <u>Cholangiocarcinoma</u> • Not reported	<u>Pancreas</u> • N=0/2 (0%) MSI-H patients <u>Gallbladder</u> • N=0/1 (0%) MSI-H patients <u>Cholangiocarcinoma</u> • N=0/8 (0%) MSI-H patients LS overall: 0%	<u>Pancreas</u> • Not reported <u>Gallbladder</u> • Not reported <u>Cholangiocarcinoma</u> • Not reported	<u>Pancreas</u> • Not reported <u>Gallbladder</u> • Not reported <u>Cholangiocarcinoma</u> • Not reported	<u>Pancreatic</u> <u>MSI-H tumours</u> • Age range: 54-67y • N=0/2 (0%) females <u>Gallbladder</u> <u>MSI-H tumours</u> • Age: 70y • N=1/1 (100%) males <u>Cholangiocarcinoma</u> <u>MSI-H tumours</u> • Age range: 51-77y • N=6/8 (75%) males
Moy (2015) • Gallbladder cancer	Retrospective cohort study • Setting: surgical pathology files of Massachusetts General Hospital, Boston • Period: 1988-2012	• MMRd in N=6/77 (7.8%)	• Lost *MLH1*/*PMS2*: N=1/6 (16.7%)	• N=0/6 (0%) MSI- patients • Overall: N=0/77 (0%)	Not reported	Not reported	<u>MSI tumours</u> • Mean age: 70.8y • N=2/6 (33.3%) males
Goeppert (2019) • Gallbladder cancer	Retrospective cohort study • Setting: University Hospital	• MSI-H: N=1/69 (1.4%) • IHC: "no loss of nuclear immunoreactivity for	Not detected	Not reported	Not reported	Not reported	<u>MSI-H tumour</u> • Age at diagnosis: 68y • N=0/1 (0%) male

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Study characteristics		Prevalence					Age and Sex
Author (year)	Study design	Overall MMRd (IHC MMR) or MSI	Loss of *MLH1*/*PMS2*, *MLH1*-PM	Germline (likely) PV MMR gene	Somatic (likely) PV MMR gene and/or LOH	UMMRd	
	Heidelberg, Germany • Period: 1995-2010	all tested repair proteins"					
Ju (2020) • Intra- and extrahepatic cholangiocarcinomas	Retrospective cohort study • Setting: institutional database (Citrix Copath and EPIC Hyperspace) • Period: 1993-2014	• Possible MMRd by IHC: N=9/96 (9.4%) • MSI: N=6/96 (6.3%) of which N=4 with MSI-H and N=2 with MSI-L. These 6 cases were grouped into the MMRd group	• Lost *MLH1*/*PMS2*: N=5/6 (83.3%), none showed *MLH1*-PM	• Not tested	Not reported	Not reported	MMRd tumours • Mean age: 68y • N=3/6 (50%) males
Ando (2022) • Biliary tract carcinomas	Retrospective cohort study • Setting: Kagawa University Hospital, Japan • Period: January 2008-December 2017	• MMRd: N=5/116 (4.3%) • MSI-H: 2/5 (40%) MMRd patients which was determined by IHC	• Lost *MLH1*/*PMS2*: N=1/5 (20%) cases of intrahepatic cholangiocarcinoma	Not reported	Not reported	Not reported	Total cohort • Median age at diagnosis: 73y (range, 38-93) • N=73/116 (62.9%) males MMRd patients • Age range: 55-93 years • N=3/5 (60%) males
Summary *Range or estimate upon availability*	-	Pancreas • MMRd: 0.8-7.5% *Sources: Hu (2018), Abrha (2020), Grant (2021)* • MSI: 1.0-4.5% *Sources: Christakis (2019), Grant (2021),*	Pancreas • *MLH1*/*PMS2*: 0-50% MMRd/MSI patients *Sources: Christakis (2019), Grant (2021), Kryklyva (2022)* • *MLH1*-PM: 23.1% *Source: Abrha (2020)*	Pancreas • Overall: 0.5-4.5% *Sources: Hu (2018), Christakis (2019), Abrha (2020), Grant (2021), Kryklyva (2022)* Gallbladder • Overall: 0%	Pancreas • 0-15.4% *Sources: Christakis (2019), Abrha (2020), Grant (2021), Kryklyva (2022)* Gallbladder Not reported Bile duct	Pancreas • 0 (MSI-patients) - 11.1% (MMRd patients) *Sources: Abrha (2020), Kryklyva (2022)* Gallbladder Not reported Bile duct	Pancreas (total cohort) • Age: 43-71y • 34-64.2% females *Sources: Christakis (2019), Mettman (2020), Kryklyva (2022)*

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Study characteristics		Prevalence					Age and Sex
Author (year)	Study design	Overall MMRd (IHC MMR) or MSI	Loss of *MLH1*/*PMS2*, *MLH1*-PM	Germline (likely) PV MMR gene	Somatic (likely) PV MMR gene and/or LOH	UMMRd	
		Kryklyva (2022), Kubo (2022) <u>Gallbladder</u> • MMRd: 2.5% *Source: Abrha (2020)* • MSI: 0-7.8% *Sources: Christakis (2019), Kubo (2022), Moy (2015), Goeppert (2019)* <u>Bile duct</u> • MMRd: 0-9.4% *Sources: Abrha (2020), Ju (2020), Ando (2022)* • MSI: 1.7-9.1% *Sources: Christakis (2019), Kubo (2022), Ju (2020), Ando (2022)* <u>Ampullary</u> • MMRd: 5.6-21.4% *Sources: Agaram (2010), Abrha (2020)* • MSI: 0-4.3% *Sources: Christakis (2019), Kryklyva (2022)*	• Isolated lost *MLH1*: 0.7% *Source: Grant (2021)* <u>Gallbladder</u> • *MLH1/PMS2*: 16.7% *Source: Moy (2015)* <u>Bile duct</u> • *MLH1/PMS2*: 20-83.3% (MMRd cases) *Sources: Ju (2020), Ando (2022)* • *MLH1*-PM: 0% *Source: Ju (2020)* <u>Ampullary</u> • *MLH1/PMS2*: 33.3-100% MMRd/MSI patients *Sources: Agaram (2010), Kryklyva (2022)* • *MLH1*-PMhm: 66.7% *Source: Abrha (2020)*	*Source: Moy (2015)* <u>Bile duct</u> • Overall: 0% *Source: Kubo (2022)* <u>Ampullary</u> • Overall: 4.3% *Source: Kryklyva (2022)*	Not reported <u>Ampullary</u> • 0% *Source: Kryklyva (2022)*	Not reported <u>Ampullary</u> • 0% *Source: Kryklyva (2022)*	<u>Gallbladder (MSI-H tumours)</u> • Age: 68-70.8y • 0-100% males *Sources: Kubo (2022), Moy (2015), Goeppert (2019)* <u>Bile duct (MSI-H tumours)</u> • Age: 51-77y • 75% males *Source: Kubo (2022)* <u>Ampullary</u> • Age: 44-64y • 37-56.5% females *Sources: Agaram (2010), Kryklyva (2022)*
Upper tract urothelial cancer (UTUC) and urothelial bladder cancer (UBC)							
Rasmussen (2022) • UTUC excluding UBC	Meta-analysis	• MMRd: 9% (range, 2.4% to 39.0%), based on N=140/1559	• Lost *MLH1*: 4.1%, based on N=67/1628 patients from 12 studies	• Suspected and verified LS: 4.7% (range, 0.8% to 13.9%), based on	Not reported	Not reported	<u>LS patients</u> • Median age at onset: 38-64y (range, 38-86)

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Study characteristics		Prevalence					Age and Sex
Author (year)	Study design	Overall MMRd (IHC MMR) or MSI	Loss of *MLH1*/*PMS2*, *MLH1*-PM	Germline (likely) PV MMR gene	Somatic (likely) PV MMR gene and/or LOH	UMMRd	
		patients from 11 studies • MSI-H: 3.9% (range, 1.7% to 13%), based on N=903 patients from 4 studies		N=51/1087 patients from 8 studies			• UTUC in females: 45% (range, 0% to 100%) among verified LS patients
Audenet (2019) • UTUC and UBC	Both retrospective and prospective cohort study • 111 samples were prospectively profiled and 84 samples retrospectively	<u>UTUC</u> • MSI-H: N=12/194 (6.2%) • MSI-H (MSI sensore score ≥10): N=10/12 (83.3%) Lynch patients; 2 with LS indeterminate MSI sensor scores (3-10) <u>UBC</u> • MSI-H: N=4/454 (0.9%)	<u>UTUC</u> Not reported <u>UBC</u> Not reported	<u>UTUC</u> • From N=47 patients consent to assess for germline mutations (MSI-H and based on family) • N=12/47 (25.5%) patients with (likely) pathogenic germline mutation • Overall: N=12/194 (6.2%) <u>UBC</u> • N=1/4 (25%) MSI patients • Overall: N=1/454 (0.2%)	<u>UTUC</u> • N=1/12 (8.3%) <u>UBC</u> • Not reported	<u>UTUC</u> • N=1/12 (8.3%) <u>UBC</u> • Not reported	<u>UTUC</u> • Median age: 67.1y (IQR, 58.1-74.5) • N=74/195 (38%) females <u>UBC</u> • Median age: 67.5y (IQR, 60.1-74.4) • N=367/454 (81%) males
Kagawa (2021) • UBC only	Retrospective cohort study • Setting: Saitama Medical Center, Japan • Period: June 1997-February 2018	• MMRd: N=9/618 (1.5%) → the 9 MMRd cases by IHC were tested for MSI • MSI-H: N=7/9 (78%) MMRd cases	• Lost *MLH1*/*PMS2*: N=3/9 (33.3%) IHC MMRd cases • *MLH1*-PM: N=0/3 (0%)	• Minimal: N=2/618 (0.6%, 95% CI: 0.1, 1.2%) • Maximal: N=7/618 (1.1%, 95% CI: 0.5, 2.3%)	Not reported	Not reported	<u>MMRd patients</u> • Median age: 68y (range, 63-79) • N=9/9 (100%) males

Bijlage: Table 2. Overview of studies on prevalences of overall MMRd, MMRd based on *MLH1* promoter methylation (*MLH1*-PM), germline or somatic (likely) pathogenic variants (PV) or unexplained MMRd (UMMRd) across different cancer types.

Study characteristics		Prevalence					Age and Sex
Author (year)	Study design	Overall MMRd (IHC MMR) or MSI	Loss of *MLH1*/*PMS2*, *MLH1*-PM	Germline (likely) PV MMR gene	Somatic (likely) PV MMR gene and/or LOH	UMMRd	
Kullmann (2023) • UTUC excluding UBC	Retrospective cohort study • Setting: archives of three collaborating institutes of Pathology: Málaga, Marburg and Erlangen • Period: 1995-2017	• MSI using Bethesda panel and Idylla assay: N=4/243 (1.6%) • MMRd: N=5/156 (3.2%)	Not reported	Not reported	Not reported	Not reported	MSI-H tumours • Age range 52 to 83y • N=1/4 (25%) females
Ma (2023) • UTUC and UBC	Retrospective cohort study • Setting: search in database of Shandong Provincial Hospital, Jinan, China • Period: 2018-2022	UTUC • MMRd: N=9/219 (3.9%) UBC • MMRd: N=1/361 (0.3%) UTUC + UBC • MMRd: N=5/13 (38.4%)	UTUC + UBC • "No cases with *MLH1* and/or *PMS2* loss were identified"	UTUC • N=5/9 (55.6%) had mutation in *MSH2* gene UBC • Not reported UTUC + UBC • N=2/5 (40%) (1 no data)	Not reported	Not reported	UTUC • Age of MMRd cases: 64y (SD 13.5) • N=7/14 (50.0%) females UBC • Age of MMRd cases: 62.3y (SD 16.7) • N=3/6 (50.0%) males
Pivovarcikova (2023) • UTUC excluding UBC	Retrospective cohort study • Setting: Šikl's Department of Pathology, Czech Republic • Period: 2010-2022	• MMRd: N=15/180 (8.3%)	• Lost *MLH1*/*PMS2*: N=3/15 (20%) • *MLH1*-PM: N=1/3 (33.3%)	• Overall: N=5/180 (2.8%), including 4 mutations in *MSH6* and 1 mutation in *MSH2*	Not reported	Not reported	• Mean age of 66.2y among 5 LS cases with UTUC • N=3/5 (60%) females

Bijlage: Table 2. Overview of studies on prevalences of overall MMRd, MMRd based on *MLH1* promoter methylation (*MLH1*-PM), germline or somatic (likely) pathogenic variants (PV) or unexplained MMRd (UMMRd) across different cancer types.

Study characteristics		Prevalence					Age and Sex
Author (year)	Study design	Overall MMRd (IHC MMR) or MSI	Loss of *MLH1*/*PMS2*, *MLH1*-PM	Germline (likely) PV MMR gene	Somatic (likely) PV MMR gene and/or LOH	UMMRd	
Summary *Range or estimate upon availability*	-	UTUC • MMRd: 3.2-9% *Sources: Rasmussen (2022), Kullmann (2023), Ma (2023), Pivovarcikova (2023)* • MSI: 1.6-6.2% *Sources: Rasmussen (2022), Audenet (2019), Kullmann (2023)* UBC • MMRd: 0.3-1.5% *Sources: Kagawa (2021), Ma (2023)* • MSI: 0.9% *Source: Audenet (2019)*	UTUC • Lost *MLH1*/*PMS2*: 0-20% *Sources: Rasmussen (2022), Pivovarcicova (2023)* • *MLH1*-PM: 33.3% *Source: Pivovarcicova (2023)* UBC • Lost *MLH1*/*PMS2*: 0% *Sources: Kagawa (2021)* • *MLH1*-PM: 0% *Source: Kagawa (2021)*	UTUC • Overall: 2.3-6.2% *Sources: Rasmussen (2022), Audenet (2019), Pivovarcicova (2023)* UBC • Overall: 0.2-1.1% *Sources: Audenet (2019), Kagawa (2021)*	UTUC • 8.3% *Source: Audenet (2019)* UBC Not reported	UTUC • 8.3% *Source: Audenet (2019)* UBC Not reported	UTUC • Age: 52-83y (MSI tumours), 64y (MMRd tumours), 67.1y (all patients) • 25% females (MSI tumours), 50% females (MMRd tumours), 38% females (all patients) *Sources: Audenet (2019), Kullmann (2023), Ma (2023)* UBC • Age: 62.3-68y (MMRd tumours), 67.5y (all patients) • 50-100% males (MMRd tumours), 81% males (all patients) *Sources: Audenet (2019), Kagawa (2021), Ma (2023)*
Small bowel cancer (SBA) and gastric cancer (GC)							
Christakis (2019) • Upper gastrointestinal tract cancers	Institutional cohort study • Setting: Dana Farber Cancer Institute, Boston, USA • Period: not reported	Small bowel • MSI: N=8/29 (28%) Gastric • MSI: N=9/97 (9%)	Small bowel • Lost *MLH1*/*PMS2*: N=4/8 (50%) MMRd patients • *MLH1*-PM: N=2/4 (50%) Gastric	Small bowel • Overall: 4/29 (13.8%) Gastric • Overall: 1/97 (1.0%)	Small bowel • N=2/8 (25%) Gastric • N=1/9 (11.1%)	Small bowel • N=0/8 (0%) Gastric • N=3/9 (33.3%)	Total cohort • Median age: 65.3y (range, 19-93.6) • N=219/645 (34%) females LS patients • Median age: 69.6y (range, 49.8-74.6)

Bijlage: Table 2. Overview of studies on prevalences of overall MMRd, MMRd based on *MLH1* promoter methylation (*MLH1*-PM), germline or somatic (likely) pathogenic variants (PV) or unexplained MMRd (UMMRd) across different cancer types.

Study characteristics		Prevalence					Age and Sex
Author (year)	Study design	Overall MMRd (IHC MMR) or MSI	Loss of *MLH1*/*PMS2*, *MLH1*-PM	Germline (likely) PV MMR gene	Somatic (likely) PV MMR gene and/or LOH	UMMRd	
			• Lost *MLH1*/*PMS2*: N=7/9 (77.8%) MMRd patients • *MLH1*PMm: N=4/7 (57.1%)				• Sex not reported
Abrha (2020) • Gastrointestinal malignancies	Retrospective cohort study • Setting: SCCI • Period: January 2016 – December 2017	<u>Small bowel</u> • MMRd: N=1/20patients (5.0%) <u>Gastric</u> • MMRd: N=15/150 (10%)	<u>Small bowel</u> • Not reported <u>Gastric</u> • *MLH1*-PM: N=11/15 (73.3%) MMRd patients	<u>Small bowel</u> • Not reported <u>Gastric</u> • N=0/15 (0%) MMRd patients (1 not tested)	<u>Small bowel</u> • Not reported <u>Gastric</u> • Double somatic: N=1/15 (6.7%) MMRd patients • Possibly double somatic: N=2/15 (13.3%) MMRd patients	<u>Small bowel</u> • Not reported <u>Gastric</u> • N=1/15 (6.7%) MMRd patients	<u>Small bowel; MMRd patients</u> • Age and sex not reported <u>Gastric; MMRd patients</u> • Median age at diagnosis: 77y (IQR, 71-86) • N=10/15 (67%) males
Aparicio (2021) • Small bowel adenocarcinoma (SBA)	Retrospective cohort study • Setting: France • Period: January 2009-December 2012	• MMRd: N=50/180 (28%) patients (66% duodenum, 22% jejunum, 12% ileum)	• Lost *MLH1*/*PMS2*: N=21/50 (42%) MMRd patients	• N=17/50 (34%) MMRd patients • Overall: N=17/180 (9.4%)	• N=113/125 (90.4%) at least one genomic alteration	Not reported	<u>MMRd tumours</u> • Median age: 58y • N=28/50 (56%) males
Latham (2021) • SBA	Retrospective cohort study • Setting: patients diagnosed with SBA at MSKCC from 2006-2019	• MMRd: N=26/100 (26%)	• Lost *MLH1* and/or *PMS2* (IHC): N=17/26 (65.4%) MMRd patients • *MLH1*-PM: N=7/9 (77.8%) LS negative SBA patients	• N=10/26 (38.5%) • Overall: N=10/100 (10%)	<u>Among n=16 LS-negative SBA patients</u> • N=2 patients declined additional work-up • N=9/14 (64.3%) had a somatic driver	Not reported	<u>Total cohort</u> • Median age: 60y • N=59/95 (62%) males <u>MMRd LS cohort</u> • Median age: 47.5y • N=5/10 (50%) males
Sanchez (2021) • SBA	Retrospective cohort study	• MMRd: N=20/94 (21.3%)	• Lost *MLH1*/*PMS2*: N=7/20 (35%) MMRd patients		Not reported	Not reported	<u>MMRd tumours</u>

Bijlage: Table 2. Overview of studies on prevalences of overall MMRd, MMRd based on *MLH1* promoter methylation (*MLH1*-PM), germline or somatic (likely) pathogenic variants (PV) or unexplained MMRd (UMMRd) across different cancer types.

Study characteristics		Prevalence					Age and Sex
Author (year)	Study design	Overall MMRd (IHC MMR) or MSI	Loss of *MLH1*/*PMS2*, *MLH1*-PM	Germline (likely) PV MMR gene	Somatic (likely) PV MMR gene and/or LOH	UMMRd	
	• Setting: 4 Spanish tertiary hospitals • Period: 2004-2020		• Isolated lost *MLH1*: N=2/20 (10%) MMRd patients	• N=9/15 (60%) with MMRd tumours that had germline testing Overall: N=9/94 (10.1%) SBAs			• Median age at diagnosis: 58y (IQR, 44.5-69) • N=12/20 (60%) males
Suerink (2021) • Small bowel cancer	Retrospective cohort study • Setting: PALGA • Period: 2012 – 2016	<u>Resections</u> • MMRd: N=74/332 (22.3%) <u>Biopsies</u> • MMRd: N=3/68 (4.4%)	<u>Resections</u> • <u>*MLH1*-PM: N=30/74 (40.5%) MMRd patients</u> <u>Biopsies</u> • <u>*MLH1*-PM: N=2/3 (66.7%) MMRd patients</u>	<u>Resections</u> • N=20/74 (27.0%) MMRd patients • Overall: N=20/332 (6.0%) <u>Biopsies</u> • N=0/3 (0%) MMRd patients • Overall: N=0/68 (0%)	<u>Resections, 2 somatic hits</u> • N=10/74 (13.5%) MMRd patients <u>Biopsies, 2 somatic hits</u> • N=0/3 (0%) MMRd patients	<u>Resections</u> • N=8/74 (10.8%) MMRd patients <u>Biopsies</u> • N=1/3 (33.3%) MMRd patients	<u>LS</u> • Mean age of 54.6y • N=13/20 (65.0%) males <u>Sporadic MMRd cancers</u> • Mean age of 68.8y • N=23/44 (52.3%) males
Kryklyva (2022) • Duodenal carcinoma	Retrospective cohort study • Setting: PALGA • Period: January 2002-December 2012	<u><50y</u> • MMRd: N=11/23 (47.8%) <u>≥50y</u> • MMRd: N=1/18 (5.6%)	<u><50y</u> • Lost *MLH1*/*PMS2*: N=3/11 (27.3%) MMRd patients <u>≥50y</u> • Lost *MLH1*/*PMS2*: N=1/1 (100%) MMRd patients	<u><50y</u> • N=5/9 (55.6%) MMRd patients (2 failed) • Overall: N=5-7/23 (22-30%) <u>≥50y</u> • N=0/1 (0%) MMRd patients	<u><50y</u> • N=2/9 (22.2%) <u>≥50y</u> • N=1/1 (100%)	Not reported	<u><50y (n=23)</u> • Age: 46y (range, 17-49) • N=15/23 (65.2%) males <u>≥50y (n=18)</u> • Age: 70y (range, 57-77) • N=13/18 (72.2%) males
de Back (2024) • Small bowel cancer	Retrospective cohort study • Setting: Netherlands Cancer Registry and PALGA • Period: 1999-2019	• MMRd: N=194/635 (30.6%)	Not reported	• N=107/194 (55%) • Overall: N=107/2697 (4%) to N=107/635 (16.9%)	Not reported	Not reported	<u>Total cohort</u> • Median age: 69y (IQR, 60-77) • N=1410/2697 (52.3%) males

Bijlage: Table 2. Overview of studies on prevalences of overall MMRd, MMRd based on *MLH1* promoter methylation (*MLH1*-PM), germline or somatic (likely) pathogenic variants (PV) or unexplained MMRd (UMMRd) across different cancer types.

Study characteristics		Prevalence					Age and Sex
Author (year)	Study design	Overall MMRd (IHC MMR) or MSI	Loss of *MLH1*/*PMS2*, *MLH1*-PM	Germline (likely) PV MMR gene	Somatic (likely) PV MMR gene and/or LOH	UMMRd	
Summary *Range or estimate upon availability*	-	Small bowel • MMRd: 4.4-47.8% *Sources: Abrha (2020), Aparicio (2021), Latham (2021), Sanchez (2021), Suerink (2021), Kryklyva (2022), de Back (2024)* • MSI: 28% *Source: Christakis (2019)* Gastric • MMRd: 10% *Source: Abrha (2020)* • MSI: 9% *Source: Christakis (2019)*	Small bowel • Lost *MLH1*/*PMS2*: 27.3-65.4% (MMRd cases) *Sources: Aparicio (2021), Latham (2021), Sanchez (2021), Kryklyva (2022)* • *MLH1*-PM: 40.5% (resections, MMRd cases), 50%, 66.7% (biopsies, MMRd cases), 77.8% (LS negative cases) *Sources: Christakis (2019), Latham (2021), Suerink (2021)* • Isolated lost *MLH1*: 10% *Source: Sanchez (2021)* Gastric • Lost *MLH1*/*PMS2*: 77.8% (MMRd cases) *Source: Christakis (2019)* • *MLH1*-PM: 57.1%, 73.3% (MMRd cases) *Sources: Christakis (2019), Abrha (2020)*	Small bowel • Overall: 0-30% *Sources: Christakis (2019), Aparicio (2021), Latham (2021), Sanchez (2021), Suerink (2021), Kryklyva (2022), de Back (2024)* Gastric • Overall: 0-1% *Sources: Christakis (2019), Abrha (2020)*	Small bowel • 0% (biopsies, MMRd cases), 13.5% (resections, MMRd cases), 22.2% (MMRd cases), 25% (MSI cases), 64.3% (LS negative cases) *Sources: Christakis (2019), Latham (2021), Suerink (2021), Kryklyva (2022)* Gastric • 6.7% (MMRd cases), 11.1% (MSI cases) *Sources: Christakis (2019), Abrha (2020)*	Small bowel • 0% (MSI cases), 10.8% (resections, MMRd cases), 33.3% (biopsies, MMRd cases) *Sources: Christakis (2019), Suerink (2021)* Gastric • 6.7% (MMRd cases), 33.3% (MSI cases) *Sources: Christakis (2019), Abrha (2020)*	Small bowel • Age: 46y (total cohort <50y), 47.5y (MMRd LS cases), 54.6y (LS cases), 58y (MMRd cases), • 50% males (MMRd LS cases), 56-60% males (MMRd cases), 65% males (LS cases), 65.2% males (total cohort <50y) *Sources: Aparicio (2021), Latham (2021), Sanchez (2021), Suerink (2021), Kryklyva (2022)* Gastric • Age: 77y (MMRd cases) • 67% males (MMRd cases) *Source: Abrha (2020)*
Brain tumors (BT)							

Bijlage: Table 2. Overview of studies on prevalences of overall MMRd, MMRd based on *MLH1* promoter methylation (*MLH1*-PM), germline or somatic (likely) pathogenic variants (PV) or unexplained MMRd (UMMRd) across different cancer types.

Study characteristics		Prevalence					Age and Sex
Author (year)	Study design	Overall MMRd (IHC MMR) or MSI	Loss of *MLH1*/*PMS2*, *MLH1*-PM	Germline (likely) PV MMR gene	Somatic (likely) PV MMR gene and/or LOH	UMMRd	
Rodriguez-Hernandez (2013) • Astrocytomas (N=20 low-grade, N=19 anaplastic, and N=57 glioblastoma)	<u>Study cohort</u> • Setting: University Hospital of Salamanca, Spain • Recruitment period: June 2000-March 2006	• MMRd: N=41/96 (43%) • MSI-H: N=4/88 (5%) → all four glioblastomas	• *MLH1*-PM: N=11/92 (12.0%) • Also, *MSH2*/*MSH6* methylation and not corresponding with IHC staining	• N=5/44 (11.4%) with MMR germline mutation • Overall: N=5/96 (5.2%) "Only one glioblastoma was associated with LS"	N=1/44 (2.3%) with MMR somatic mutation	N=27/44 (61.4%)	<u>Low-grade</u> • Median age: 35y (IQR, 30.3-46.0) • N=11/20 (55%) males <u>Anaplastic</u> • Median age: 57y (IQR, 47.0-66.0) • N=12/19 (63%) males <u>Glioblastoma</u> • Median age: 63y (IQR, 54.5-69.0) • N=36/57 (63%) males
Hadad (2023) • Glioblastoma	• Setting: University of California, San Francisco • Period: 2017-2022	• MSI-H by NGS: N= 9/459 (2.0%)	Not reported	• N=4/9 (44.4%) MSI-H patients • Overall: N=4/459 (0.9%)	N=3/9 (33.3%) or N=3/459 (0.65%) with somatic mutations	Not reported	<u>De novo RRD GBM, IDH-wildtype</u> • Mean age: 50y (IQR, 40-57) • N=3/9 (33.3%) males
Summary *Range or estimate upon availability*	-	<u>Astrocytomas</u> • MSI: 5% *Source: Rodriguez-Hernandez (2013)* <u>Glioblastoma</u> • MSI: 2% *Source: Hadad (2023)*	<u>Astrocytomas</u> • *MLH1*-PM: 12% *Sources: Rodriguez-Hernandez (2013)* <u>Glioblastoma</u> Not reported	<u>Astrocytomas</u> • Overall: 5.2% *Source: Rodriguez-Hernandez (2013)* <u>Glioblastoma</u> • Overall: 0.9% *Source: Hadad (2023)*	<u>Astrocytomas</u> • 2.3% *Source: Rodriguez-Hernandez (2013)* <u>Glioblastoma</u> • 0.65% *Source: Hadad (2023)*	<u>Astrocytomas</u> • 61.4% *Source: Rodriguez-Hernandez (2013)* <u>Glioblastoma</u> Not reported	<u>Glioblastoma</u> • Age: 50-63y • 33.3% males (MSI cases), 63% males (total cohort) *Sources: Rodriguez-Hernandez (2013), Hadad (2023)*
Sebaceous gland tumor (SGT)							
Kunnackal John (2022) • Sebaceous tumors	Meta-analysis	52.5% (95% CI 48.74% to 56.26%), based on	Not reported	18.8% (95% CI 13.03% to 24.57%), based on	Not reported	Not reported	Age and sex not reported

Bijlage: Table 2. Overview of studies on prevalences of overall MMRd, MMRd based on *MLH1* promoter methylation (*MLH1*-PM), germline or somatic (likely) pathogenic variants (PV) or unexplained MMRd (UMMRd) across different cancer types.

Study characteristics		Prevalence					Age and Sex
Author (year)	Study design	Overall MMRd (IHC MMR) or MSI	Loss of *MLH1*/*PMS2*, *MLH1*-PM	Germline (likely) PV MMR gene	Somatic (likely) PV MMR gene and/or LOH	UMMRd	
		N=355/676 patients from 10 studies		N=33/176 patients from 2 studies			
Cook (2023) • Sebaceous tumors	Retrospective cohort study • Setting: National Cancer Registration and Analysis Service, England • Period:	• MMR IHC performed in N=220/1077 (20%) of tumours • MMRd: N=70/220 (32%)	• Lost *MLH1*/*PMS2*: N=15/70 (21.4%) MMRd patients	• N=12/24 (50%) tested patients • Overall: N=12/220 (5.5%)	Not reported	Not reported	<u>Total cohort</u> • Median age at diagnosis: 76y (IQR: 17) • N=632/1077 (58.7%) males
Kattapuram (2023) • Sebaceous lesions	Retrospective cohort study • Setting: University of Michigan • Period: January 2009-December 2019	• IHC conducted in N=173/427 (41%)patients • N=92/173 (53%) with abnormal staining (n=20 known LS cases excluded)	• Lost *MLH1*/*PMS2*: N=13/92 (14.1%) patients with abnormal staining • "No patient underwent *MLH1*-PM testing"	• N=69 abnormal IHC staining referred to genetics • Overall: N=6 newly diagnosed → N=6/69 (9%); N=20 with existing LS → N=26/69 (37.7%)	Not reported	Not reported	<u>Total cohort</u> • Mean age at diagnosis: 69.3y (SD 12.4) • N=281/447 (63%) males <u>LS patients</u> • Mean age at diagnosis: 59.7y (SD 10.9) • N=15/27 (56%) males
Sinson (2023) • Sebaceous lesions	Retrospective cohort study • Setting: pathological laboratories in the Poitou-Charentes region of France • Period: 2004-2017	• MMRd: N=87/123 (70.7%) of tumours • MSI: N=59/123 (47.8%)	• Lost *MLH1*/*PMS2*: N=12/123 (9.8%) sebaceous lesions • *MLH1*-PM: N=0/12 (0%)	• Overall: N=25/123 (20.3%) tumours (not all tumours tested)	Not reported	Not reported	<u>All histological subtypes</u> • Mean age: 71.1y (range, 30-96) • Sex ratio (M:W): 1.7

Bijlage: Table 2. Overview of studies on prevalences of overall MMRd, MMRd based on *MLH1* promoter methylation (*MLH1*-PM), germline or somatic (likely) pathogenic variants (PV) or unexplained MMRd (UMMRd) across different cancer types.

Study characteristics		Prevalence					Age and Sex
Author (year)	Study design	Overall MMRd (IHC MMR) or MSI	Loss of *MLH1*/*PMS2*, *MLH1*-PM	Germline (likely) PV MMR gene	Somatic (likely) PV MMR gene and/or LOH	UMMRd	
Summary *Range or estimate upon availability*	-	• MMRd: 32-70.7% *Sources: Kunnackal John (2022), Cook (2023), Kattapuram (2023), Sinson (2023)* • MSI: 47.8% *Source: Sinson (2023)*	• Lost *MLH1*/*PMS2*: 14.1%, 21.4% (MMRd cases), 9.8% (all cases) *Sources: Cook (2023), Kattapuram (2023), Sinson (2023)* • *MLH1*-PM: 0% *Source: Sinson (2023)*	• Overall: 5.5%, 9%, 18.8% *Sources: Kunnackal John (2021), Cook (2023), Kattapuram (2023)*	Not reported	Not reported	• Age: 69.3-76y • 58.7-63% males *Sources: Cook (2023), Kattapuram (2023), Sinson (2023)*
Prostate cancer (PRC)							
Abida (2019) • Prostate cancer	Case series • Setting: prospective analysis of patients with prostate cancer undergoing treatment at MSKCC, New York • Period: January 2015-Januari 2018	• MSI-H: N=32/1033 (3.1%)	Not reported	• N=7/32 (21.9%) MSI-H patients • Overall: N=7/1033 (0.68%)	• N=6/1033 (0.6%) with somatic alteration, but without evidence of MSI or hypermutation	Not reported	<u>MSI-H cohort</u> • Median age at diagnosis: 64.5y (range, 39-85) • 100% males
Pritzlaff (2020) • Prostate cancer	Clinical lab cohort • Setting: Ambry genetics, USA • Period: April 2012-September 2017	• MMRd: 2.8%	<u>No prior genetic testing</u> • Isolated *MLH1* loss: N=2/1501 (0.1%) tested patients	<u>No prior genetic testing</u> • N=26/1501 (1.7%)	Not reported	Not reported	<u>Total cohort</u> • Median age at diagnosis: 60y (IQR 54-66) • 100% males

Bijlage: Table 2. Overview of studies on prevalences of overall MMRd, MMRd based on *MLH1* promoter methylation (*MLH1*-PM), germline or somatic (likely) pathogenic variants (PV) or unexplained MMRd (UMMRd) across different cancer types.

Study characteristics		Prevalence					Age and Sex
Author (year)	Study design	Overall MMRd (IHC MMR) or MSI	Loss of *MLH1*/*PMS2*, *MLH1*-PM	Germline (likely) PV MMR gene	Somatic (likely) PV MMR gene and/or LOH	UMMRd	
Kagawa (2021) • Prostate cancer	Retrospective cohort study • Setting: Saitama Medical Center and Saitama Medical University, Japan • Period: Januari 2001-May 2016	• MMRd: N=4/337 (1.2%)	Not present	• N=0/2 (0%) that were tested• Overall: N=0/337 (0%)	• N=2/4 at least one somatic alteration inactivating *MSH2* without *MSH2* hypermethylation was identified	• N=2/337 (0.6%) with supposed Lynch-like syndrome	<u>Total cohort</u> • Median age: 67y (range, 52-81) • 100% males <u>MMRd patients</u> • Age range: 64-75y • 100% males
Oka (2023) • Prostate cancer	Retrospective cohort study • Setting: Toranomon Hospital, Tokyo, Japan • Period: 2012-2015	• MMRd: N=1/129 (0.8%)	Not present	• N=1/129 (0.8%)	Not reported	Not reported	<u>Total cohort</u> • Median age at diagnosis: 68y (range, 52-79) • 100% males <u>MMRd patient</u> • Age: 68y • 100% male
Truong (2023) • Prostate cancer	Retrospective cohort study • Setting: MSKCC • Period: 2015-2020	• N=1883 patients included in study • MSI status available in n=1603 tumours • MSI-H: N=35/1603 (2.2%)	• Lost *MLH1*: N=0/3 (0%)	• N=6/35 (17%) MSI-H patients • Overall: N=6/1605 (0.4%) • N=8 germline carriers without MSI-H tumour	Not reported	Not reported	<u>Total cohort</u> • Median age at diagnosis: 62y (IQR, 56-68) • 100% males
Summary *Range or estimate upon availability*	-	• MMRd: 0.8-2.8% *Sources: Pritzlaff (2020), Kagawa (2021), Oka (2023)* • MSI: 2.2-3.1% *Sources: Abida (2019), Truong (2023)*	• Isolated lost *MLH1*: 0-0.1% *Sources: Pritzlaff (2020), Truong (2023)*	• Overall: 0-1.7% *Sources: Abida (2019), Pritzlaff (2020), Kagawa (2021), Oka (2023), Truong (2023)*	• 0.59-0.6%, *Sources: Abida (2019), Kagawa (2021)*	• 0.6% *Source: Kagawa (2021)*	• Age: 60-68y (all cases), 64.5y (MSI-H cases), 64-75y (MMRd cases) • 100% males *Sources: Abida (2019), Pritzlaff (2020),*

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Study characteristics		Prevalence					Age and Sex
Author (year)	Study design	Overall MMRd (IHC MMR) or MSI	Loss of *MLH1*/*PMS2*, *MLH1*-PM	Germline (likely) PV MMR gene	Somatic (likely) PV MMR gene and/or LOH	UMMRd	
							Kagawa (2021), Oka (2023), Truong (2023)

Abbreviations: MMRd, mismatch repair deficiency; IHC, immunohistochemistry; UMMRd, unexplained mismatch repair deficiency; *MLH1*-PM, *MLH1* promoter methylation; LS, Lynch syndrome; MSI(-H), microsatellite instability (- high); EOC, epithelial ovarian carcinoma; PDAC, Pancreatic ductal cancer, BTC, biliary tract cancer; GBC, gallbladder cancer; UTUC, upper tract urothelial cancer; UBC, urothelial bladder cancer; SBA, small bowel adenocarcinoma; GC, gastric Cancer; BT, brain tumor; SGT, sebaceous gland tumor; PRC, prostate cancer; NGS, next generation sequencing; WGS, whole generation sequencing; IQR, interquartile range; SD, standard deviation; MSKCC, Memorial Sloan-Kettering Cancer Center; USA, United States of America; SCCI, Stanford Comprehensive Cancer Institute; KHBO, Kansai Hepato-Biliary Oncology Group; PALGA, Nationwide Network and Registry of Histopathology and Cytopathology in the Netherlands; De novo RRD GBM, de novo replication repair deficient glioblastoma.

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