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Real-world prevalence of MSI-H/dMMR across 6 different tumor types in Asia

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Background

- The anti–PD-1 monoclonal antibody pembrolizumab has tumor-agnostic approvals in the United States, Japan, and several other regions in Asia for previously treated advanced tumors characterized as microsatellite instability-high (MSI-H)/mismatch repair–deficiency (dMMR) and in the European Union and specific regions in Asia for select MSI-H/dMMR tumors[1-3]
- The global prevalence of MSI-H/dMMR in patients with advanced solid tumors is widely reported as ranging from 3% to 9%[4,5]
- In patients from Asia, real-world data on the prevalence of MSI-H/dMMR across advanced solid tumors, excluding colorectal cancer, are limited
  - Determining the prevalence of MSI-H/dMMR in different tumor types is important for informing treatment decisions in the clinical setting

Objectives

- To evaluate the real-world prevalence of MSI-H/dMMR across 6 tumor types in Asia
- To describe the clinicopathologic characteristics and treatment patterns for patients with MSI-H/dMMR and non-MSI-H/proficient mismatch repair (pMMR) tumors

Methods

Figure 1. Study design and analyses

29 study sites
Asia-Pacific
(South Korea, Singapore, Taiwan) and Japan

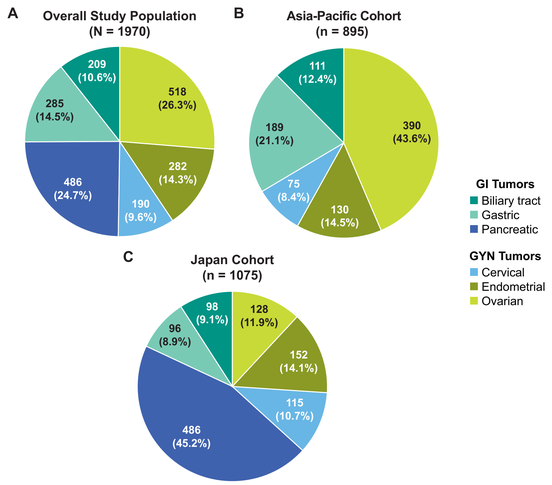
Key eligibility criteria
- All sites
  - Histologically or cytologically documented advanced (stage III/IV) endometrial, ovarian, cervical, biliary tract, or gastric cancer
  - Available tumor tissue sample collected at advanced diagnosis and ≤3 years old for biomarker testing
  - Available medical history documented ≤3 months prior to date of pathology diagnosis
- Asia-Pacific cohort only
  - Aged ≥18 years
  - Treatment-naive or previously treated tumor
- Japan cohort only
  - Aged ≥20 years
  - Histologically or cytologically documented advanced (stage III/IV) pancreatic cancer
  - Disease progression or relapse after SOC treatment

Biomarker testing
- Asia-Pacific cohort only
  - Archival FFPE tissue samples using Ventana MMR RxDx Panel
- Japan cohort only
  - Retrospective data of MSI status via FALCO PCR Test

FFPE, formalin-fixed paraffin-embedded; PCR, polymerase chain reaction; SOC, standard-of-care.

Results

Figure 2. Patient enrollment in the (A) overall study population, (B) Asia-Pacific cohort, and (C) Japan cohort



GI, gastrointestinal; GYN, gynecologic.
Patients with pancreatic cancer were enrolled only in Japan.

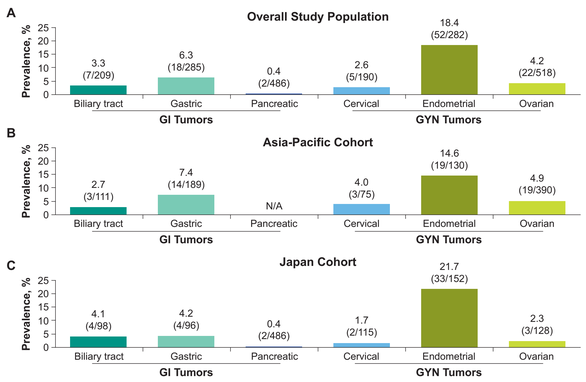
Table 1. Baseline characteristics

	Overall population N = 1970	MSI-H/dMMR population n = 106	Non-MSI-H/pMMR population n = 1864
Age			
18-65 years	1168 (59.3)	72 (67.9)	1096 (58.8)
>65 years	802 (40.7)	34 (32.1)	768 (41.2)
Sex			
Male	592 (30.1)	21 (19.8)	571 (30.6)
Female	1378 (69.9)	85 (80.2)	1293 (69.4)
ECOG PS at diagnosis			
0	1388 (70.5)	80 (75.5)	1308 (70.2)
1	413 (21.0)	18 (17.0)	395 (21.2)
≥2	61 (3.1)	5 (4.7)	56 (3.0)
Unknown	108 (5.5)	3 (2.8)	105 (5.6)
TNM stage at diagnosis			
III	842 (42.7)	53 (50.0)	789 (42.3)
IV	836 (42.4)	46 (43.4)	790 (42.4)
Unknown[a]	292 (14.8)	7 (6.6)	285 (15.3)

ECOG PS, Eastern Cooperative Oncology Group performance status; TNM, tumor, node, and metastasis staging classification.
Values are n (%) unless otherwise specified.
[a]TNM staging was not performed when patients presented with advanced disease.

- The prevalence of MSI-H/dMMR was 5.4% (106 of 1970 patients) overall, and ranged from 0.4% to 18.4% among the 6 different tumor types evaluated in this study

Figure 3. Prevalence of MSI-H/dMMR by tumor type in the (A) overall study population, (B) Asia-Pacific cohort, and (C) Japan cohort



Patients with pancreatic cancer were enrolled only in Japan.

Table 2. Prevalence of MSI-H/dMMR by tumor type across baseline characteristics in the overall study population

	Biliary tract n = 209	Gastric n = 285	Pancreatic n = 486	Cervical n = 190	Endometrial n = 282	Ovarian n = 518
Age						
18-65 years	2.4 (2/85)	4.3 (6/138)	0.5 (1/207)	3.1 (5/159)	21.2 (41/193)	4.4 (17/386)
>65 years	4.0 (5/124)	8.2 (12/147)	0.4 (1/279)	0 (0/31)	12.4 (11/89)	3.8 (5/132)
Sex						
Male	4.0 (5/126)	7.2 (14/195)	0.7 (2/271)	NA	NA	NA
Female	2.4 (2/83)	4.4 (4/90)	0 (0/215)	2.6 (5/190)	18.4 (52/282)	4.2 (22/518)
ECOG PS at diagnosis						
0	3.4 (4/119)	6.4 (11/171)	0.3 (1/392)	3.5 (5/142)	19.7 (41/208)	5.1 (18/356)
1	5.1 (3/59)	9.3 (5/54)	0 (0/87)	0 (0/38)	11.1 (6/54)	3.3 (4/121)
≥2	0 (0/8)	9.1 (1/11)	0 (0/5)	0 (0/4)	40.0 (4/10)	0 (0/23)
Unknown	0 (0/23)	2.0 (1/49)	50.0 (1/2)	0 (0/6)	10.0 (1/10)	0 (0/18)
TNM stage at diagnosis						
III	2.9 (2/69)	6.0 (10/168)	1.0 (1/101)	3.0 (2/66)	22.1 (29/131)	2.9 (9/307)
IV	3.4 (4/119)	6.2 (6/97)	0.4 (1/237)	2.9 (2/68)	17.5 (21/120)	6.2 (12/195)
Unknown[a]	4.8 (1/21)	10.0 (2/20)	0 (0/148)	1.8 (1/56)	6.5 (2/31)	6.3 (1/16)
Tumor grade at diagnosis						
Well differentiated	0 (0/17)	0 (0/22)	0 (0/33)	0 (0/8)	28.6 (14/49)	7.1 (1/14)
Moderately differentiated	4.9 (4/81)	7.3 (6/82)	1.0 (1/97)	3.1 (1/32)	12.5 (6/48)	9.1 (5/55)
Poorly differentiated	5.1 (2/39)	6.4 (10/156)	0 (0/35)	5.9 (2/34)	23.7 (23/97)	4.2 (13/311)
Unknown	1.4 (1/72)	8.0 (2/25)	0.3 (1/321)	1.7 (2/116)	10.2 (9/88)	2.2 (3/138)

NA, not applicable.
Values are % (n/N).
[a]TNM staging was not performed when patients presented with advanced disease.

Table 3. Treatment pattern at any point since initial diagnosis

	Overall study population N = 1970	MSI-H/dMMR population n = 106	Non-MSI-H/pMMR population n = 1864
Surgery	1216 (61.7)	79 (74.5)	1137 (61.0)
Radiation	400 (20.3)	27 (25.5)	373 (20.0)
Chemotherapy	1889 (95.9)	101 (95.3)	1788 (95.9)
Targeted therapy	570 (28.9)	20 (18.9)	550 (29.5)
ICI	170 (8.6)	36 (34.0)[a]	134 (7.2)

ICI, immune checkpoint inhibitor.
Values are n (%).
[a]77.8% of patients received ICIs in the second-line or later setting.

Conclusions

- The prevalence of MSI-H/dMMR ranging from 0.4% to 18.4% across the 6 tumor types in this analysis of Asian patients was consistent with the ranges reported in the literature[4-7]
- The prevalence of MSI-H/dMMR was similar across the different baseline characteristic subgroups
- A greater proportion of patients with MSI-H/dMMR tumors received treatment with ICIs compared with patients with non-MSI-H/pMMR tumors
- These data of MSI-H/dMMR prevalence reinforces the importance of biomarker testing to inform immunotherapy treatment decisions in clinical practice

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