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Characteristics and outcomes of real-world patients with MSI-H solid tumors treated with pembrolizumab

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SITUATION

May 2017: FDA approves pembrolizumab monotherapy — the first tumor-agnostic, biomarker based therapy in oncology for patients with microsatellite instability high (MSI-H) or mismatch repair deficient tumors.

As tumor-agnostic therapies are a new treatment paradigm, it is important to assess their use and effectiveness in routine clinical practice.

APPROACH

This study examined characteristics and outcomes in a cohort of patients with solid tumors identified as MSI-H who received their first pembrolizumab treatment after May 2017.

The FH-FMI CGDB, a pan-tumor linked clinical and genomic database, was used to observe pembrolizumab usage across 36 different histologies.

METHODS

Cohort Selection
Patients with MSI-H solid tumors who received pembrolizumab after May 2017.

Treatment Sequencing
We developed a structured treatment block heuristic to derive treatment sequencing in this pan-tumor cohort.

Outcomes Analyses
Overall survival & time to treatment discontinuation were evaluated with Kaplan-Meier analyses of all patients and patients with the most common tumors.

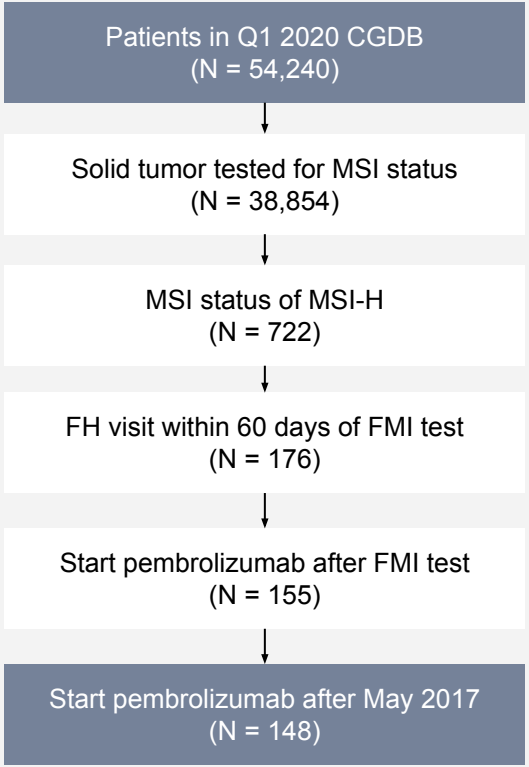

Fig 1. Patient selection

RESULTS

Table 1. Baseline characteristics

		All [N=148]	CRC [N=43]	Endometrial [N=43]	Gastric/GEJ [N=19]	Other [N=43]*
Age at pembro Initiation, Median[IQR]		69.0 [58.0;75.2]	70.0 [57.0;78.0]	67.0 [58.0;72.0]	71.0 [64.0;80.0]	68.0 [57.5;74.0]
Female gender, n (%)		96 (64.9%)	24 (55.8%)	43 (100%)	7 (36.8%)	22 (51.2%)
Last ECOG around pembro start, n (%)	0-1	57 (78.3%)	29 (87.9%)	18 (58.1%)	15 (93.8%)	28 (80.0%)
	2+	25 (21.7%)	4 (12.1%)	13 (41.9%)	1 (6.25%)	7 (20.0%)
	Missing	33 (22.3%)	10 (23.3%)	12 (27.9%)	3 (15.8%)	8 (18.6%)
Has any MMR gene Alteration, n (%)		62 (41.9%)	20 (46.5%)	13 (30.2%)	6 (31.6%)	23 (53.5%)
TMB Score, Median [IQR]		32.2 [21.3;46.9]	42.6 [31.0;55.5]	19.1 [16.0;29.4]	40.0 [32.6;48.1]	31.5 [24.2;41.3]
Follow-up from pembro start, Median [IQR]		8.28 [2.30;14.1]	7.95 [2.37;13.0]	9.36 [3.04;18.6]	7.82 [1.91;9.74]	7.16 [1.94;14.4]

*Tumors included [largest to smallest]: Occult/Unknown Primary, Prostate, Breast, Cervical, Small Intestine, Gallbladder, Lung

RESULTS

Table 2. 12-month OS in pembrolizumab treated patients with MSI-H tumors.

> Real-world 1-year overall survival (OS) rate, measured using Kaplan-Meier analysis, was **consistent with pembrolizumab trial outcomes** across all patients and largest tumor groups.

	Total N	N at risk at 12-mos	12-mos OS, % [95% CI]
All Patients	148	49	62.0 [53.4-71.9]
Colorectal	43	13	69.9 [54.5-89.6]
Endometrial	43	16	61.9 [47.1-81.4]
Gastric/GEJ	19	4	46.4 [24.2-89.0]
Other*	43	16	59.7 [45.6-78.1]

*Tumors included [largest to smallest]: Occult / Unknown Primary, Prostate, Breast, Cervical, Small Intestine, Gallbladder, Lung

IMPACT

CLINICAL IMPLICATIONS

Describes how the first tumor-agnostic, biomarker-driven FDA approval in oncology is being translated into routine clinical practice and **supports the adoption of novel tumor-agnostic cancer treatments.**

Provides supportive real-world evidence of the clinical trial data in a rare cohort where additional trials would be challenging to conduct.

DATA IMPLICATIONS

Demonstrates the ability to **evaluate complex genomic biomarkers in a pan-tumor, real-world cohort.**

Advances our understanding of pan-tumor cohort selection and outcomes analyses.

LIMITATIONS

This study relied on structured EHR-derived data, and as such, some unstructured data elements (e.g. date of diagnosis, stage, non-FMI/MSI dMMR test results) were not available.

In addition, treatment sequencing following the structured treatment block heuristic may differ from tumor-specific line of therapy rules in some cases.

MITIGATIONS

Since the time of this research, **a tumor-agnostic enhanced data model** has been built, which includes additional foundational variables from unstructured data (such as date of diagnosis and group stage) now abstracted at scale in the CGDB, making pan-tumor outcomes analyses more robust.

Efforts are underway to continue to develop tumor-agnostic data elements and analytical considerations.

THANK YOU

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