# Oncologists' Perceptions of Nivolumab Plus Ipilimumab as First-Line Treatment for Microsatellite Instability-High/Mismatch Repair-Deficient Metastatic Colorectal Cancer

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## Background

- Nivolumab plus ipilimumab (NIVO + IPI) are FDA-approved for patients with microsatellite instability-high/mismatch repair-deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC) with disease progression after chemotherapy treatment.[1]
- Compared with patients with microsatellite stable/mismatch repair-proficient mCRC, those diagnosed with MSI-H/dMMR mCRC have poorer outcomes after treatment with chemotherapy and therefore may benefit from a different frontline regimen.[2,3]
- The CheckMate 8HW (NCT04008030) trial[4] is a randomized phase III study comparing NIVO + IPI versus chemotherapy in patients with MSI-H/dMMR mCRC. It evaluates progression-free survival (PFS) by blinded independent central review (BICR) at a prespecified interim analysis for NIVO + IPI versus chemotherapy in the first-line (1L) setting.
- The CheckMate 8HW trial demonstrates superior PFS, and fewer grade 3-4 treatment-related adverse events for NIVO + IPI versus chemotherapy in previously untreated patients with MSI-H/dMMR mCRC.[5]

## Objective

- This study aimed to understand oncologists' perceptions of the phase III CheckMate 8HW trial data and its impact to patient care in the near future.

## Methods

- In a live meeting in April 2024, using an audience response system and verbal dialogue, U.S.-based oncologists were queried on their perceptions of the CheckMate 8HW trial data and anticipated NIVO + IPI use for 1L treatment of MSI-H/dMMR mCRC.
  - Not all physician attendees answered every question.
  - Demographic data were collected prior to the summit via an online survey.
- Data were analyzed using descriptive statistics.

## Results

- There were 54 practicing oncologists in the meeting with a mean of 20 years in practice; 77% were in community settings, and they were geographically dispersed (**Table 1**).
- Of these 54 providers, 89% managed colorectal cancer and had an average of 30 current and 7 referred colorectal patients in a typical 3-month period (**Table 2**).
- Following the CheckMate 8HW trial data presentation, preference for NIVO + IPI regimen as 1L therapy for a hypothetical 65-year-old male patient with an Eastern Cooperative Oncology Group performance status (ECOG PS) of 1, a KRAS mutation, and MSI-H/dMMR mCRC increased by 66 percentage points (20% to 86%) among respondents (**Figure 1**).
- Most (83%) found the 24-month progression-free survival (PFS) rates for NIVO + IPI versus chemotherapy to be the most clinically meaningful data (**Figure 2**).

**Table 1: Physician demographics and characteristics**

| | Physicians (N=54) |
|---|---|
| **Region of practice (n, %)*** | |
| South | 15 (28) |
| Midwest | 18 (33) |
| West | 8 (15) |
| Northeast | 13 (24) |
| **Primary medical specialty (n, %)** | |
| Medical oncology | 33 (61) |
| Hematology oncology | 20 (37) |
| Other: Radiation oncology | 1 (2) |
| **Years in practice** | |
| Mean (min-max) | 20 (3-45) |
| **Community-based practice (n, %)** | |
| Yes | 42 (77) |
| No | 12 (23) |

*__Midwest__: Iowa, Illinois, Indiana, Kansas, Michigan, Minnesota, Missouri, North Dakota, Nebraska, Ohio, South Dakota, Wisconsin; __Northeast__: Connecticut, Delaware, Massachusetts, Maine, Maryland, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont; __South__: Alabama, Arkansas, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, West Virginia; __West__: Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, New Mexico, Nevada, Oregon, Utah, Washington, Wyoming.

**Table 2: Number of patients currently under management and referred for management in a typical quarter**

*Question: Please estimate the number of patients with colorectal cancer you are currently treating or referred to you in a typical quarter.*

| | Current colorectal cancer patients (N=48)* | Referred colorectal cancer patients (N=48)* |
|---|---|---|
| **Average** | 30 | 7 |
| **Minimum** | 2 | 0 |
| **Maximum** | 200 | 30 |
| **Median** | 19 | 5 |

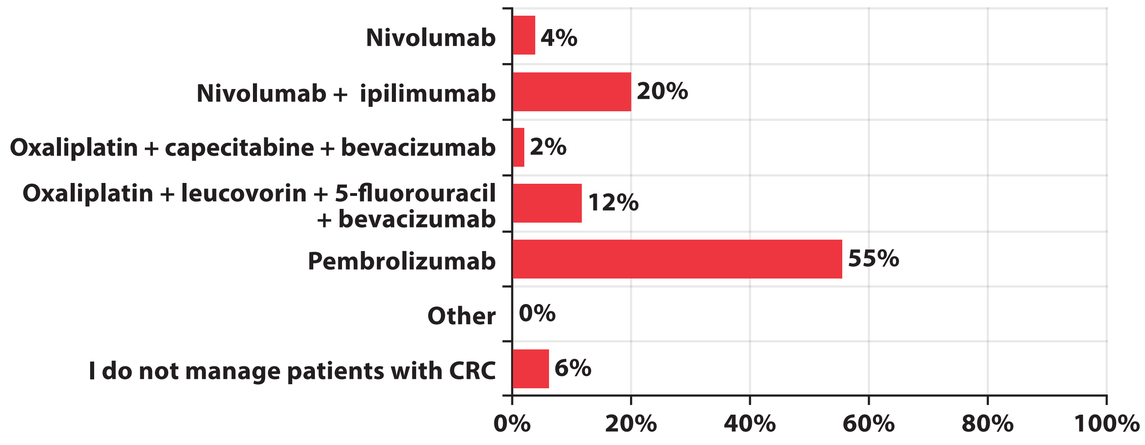
*Not all participants selected every option, sample size based on current malignancies managed.

## Results, continued

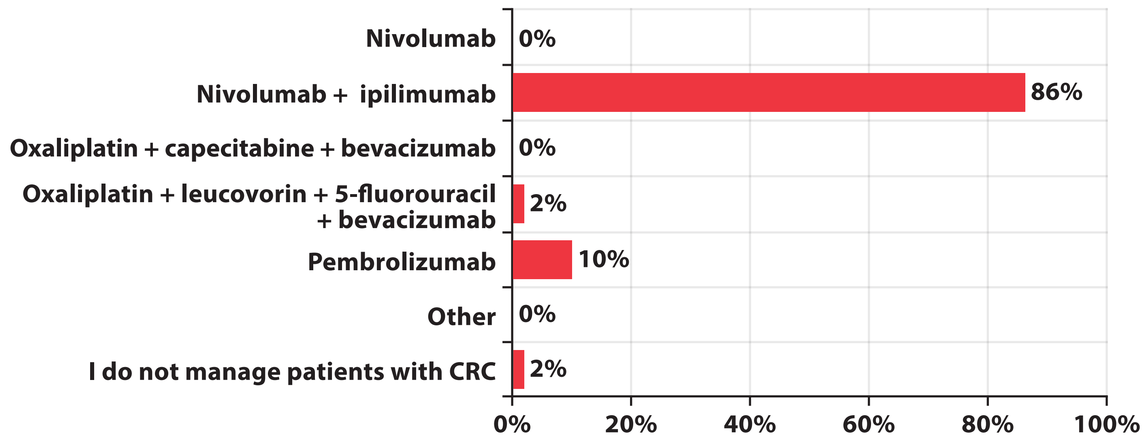
**Figure 1: Preferred prescribing behavior prior to and after review of the CheckMate 8HW trial***

*Question: What is your preferred **1L therapy** for a 65-year-old male patient with an ECOG PS of 1, a* KRAS *mutation, and MSI-H/dMMR mCRC? (Asked before and after reviewing the CheckMate 8HW results and assuming FDA approval and/or guideline recommended)*

**Prior to review of CheckMate 8HW data, n=49**



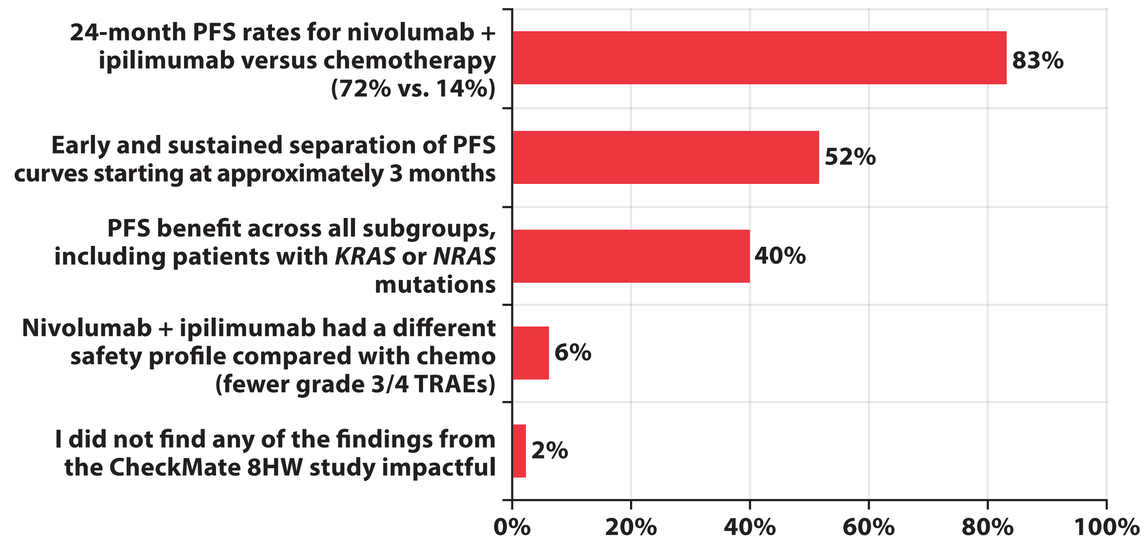

**After review of CheckMate 8HW data, n=51**




*Percentages do not sum to 100 due to rounding.

**Figure 2: Impact of trial data on physicians' management of CRC**

*Question: Which of the following findings from the CheckMate 8HW study do you find most clinically meaningful for the management of CRC? Please select up to 2. (n=52)*




## Conclusions

- Our study demonstrated that reviewing the CheckMate 8HW trial data, led to a higher preference for the use of dual checkpoint inhibition of PD-1 and CTLA4 compared to single agent immunotherapy for treatment-naïve patients with MSI-H/dMMR mCRC in 1L setting, suggesting that reviewing scientific evidence from clinical research can influence prescribing patterns.
- Insights from our study highlight the importance of reviewing and discussing clinical research data at scientific forums such as summits. It expedites physicians' knowledge of new, efficacious treatment options which allows for more informed clinical care and treatment decision-making.
- Staying updated with the latest medical advancements is crucial in ensuring that patients receive the most appropriate care available.

## References

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5. Thierry Andre et al., Nivolumab (NIVO) plus ipilimumab (IPI) vs chemotherapy (chemo) as first-line (1L) treatment for microsatellite instability-high/mismatch repair-deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC): First results of the CheckMate 8HW study. *JCO* 42, LBA768-LBA768(2024).

***Abbreviations***

1L, first-line; CRC, colorectal cancer; dMMR; deficient mismatch repair; ECOG, Eastern Cooperative Oncology Group; *KRAS*, Kirsten rat sarcoma viral oncogene homolog; mCRC, metastatic colorectal cancer; MSI-H, microsatellite instability-high; *NRAS*, Neuroblastoma rat sarcoma viral oncogene homolog; PFS, progression-free survival; PS, performance status; TRAE, treatment-related adverse event.

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