ASSOCIATION OF COMMUNITY CANCER CENTERS

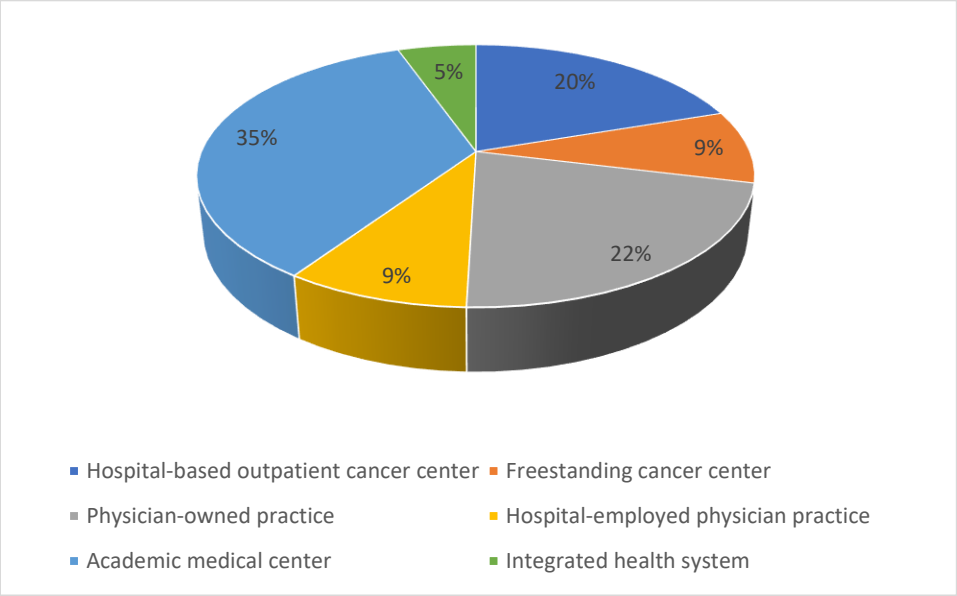
Assessing the Status of Biomarker Testing in Metastatic Colorectal Cancer and the Challenges Faced by Community Cancer Care Teams

Summary of Survey Findings
February 2021

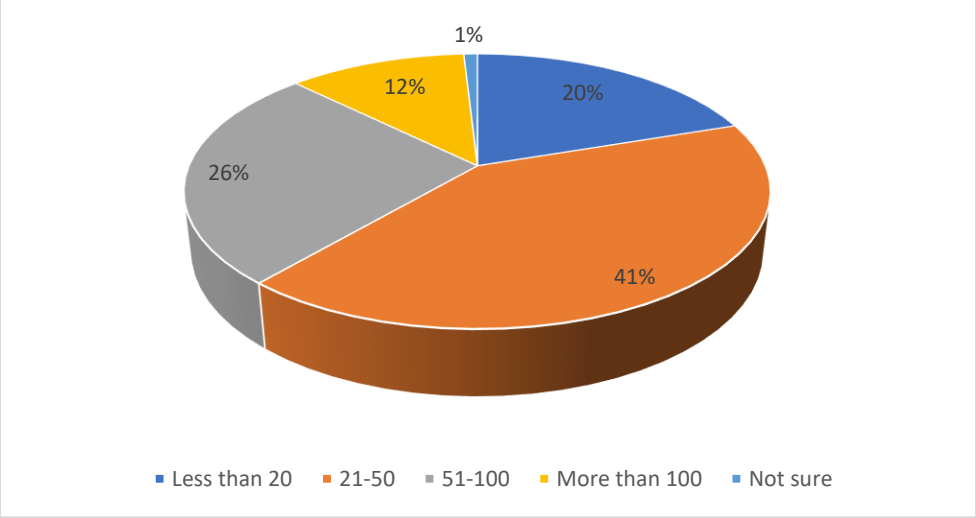
Association of Community Cancer Centers

In January 2021, the Association of Community Cancer Centers (ACCC) surveyed 111 community oncology practitioners around the U.S. to assess the status of biomarker testing in patients with metastatic colorectal cancer and the challenges faced by cancer care teams. Following is a summary of survey data collected. [Editor's note: Due to rounding, figures presented in this report may not add to 100%.]

Which of the following best describes your institution?



Approximately how many patients with unresectable or metastatic colorectal cancer (mCRC) does your cancer program treat each month?



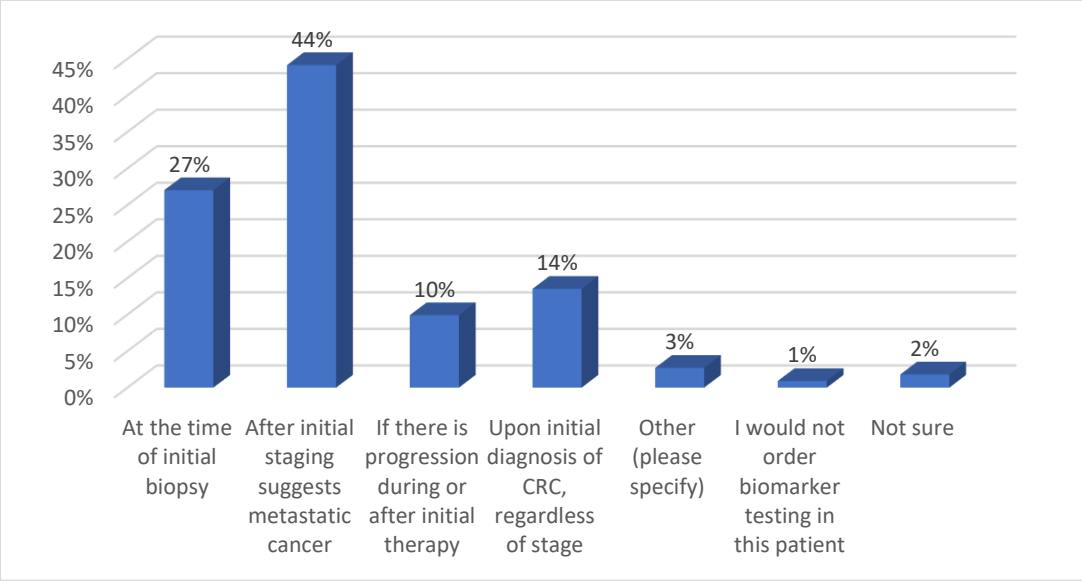
Among the cancer centers surveyed, 26% of practitioners reported treating between 50 and 100 patients with unresectable or mCRC per month, and 12% reported treating in excess of 100 such patients per month.

What guidelines/opinions do you follow when ordering biomarker testing? (Select all that apply.)

National Comprehensive Cancer Network (NCCN)	66%
American Society of Clinical Oncology (ASCO)	45%
American Society for Clinical Pathology, College of American Pathologists, Association for Molecular Pathology, and ASCO	32%
A protocol developed by your institution/multidisciplinary team	14%
No specific guidelines	5%

When questioned about the biomarker testing guidelines they follow, many respondents reported following one or more. Sixty-six percent of respondents indicated that they follow guidelines developed by the National Comprehensive Cancer Network (NCCN), 45% said they follow American Society of Clinical Oncology (ASCO) guidelines, and 32% said they follow the 2017 guideline jointly developed by the American Society for Clinical Pathology, the College of American Pathologists, the Association for Molecular Pathology, and ASCO. Fourteen percent said they employ a protocol developed by their institution or multidisciplinary team for ordering biomarker testing, and 5% reported using no specific guidelines for biomarker testing for the evaluation of patients with colorectal cancer.

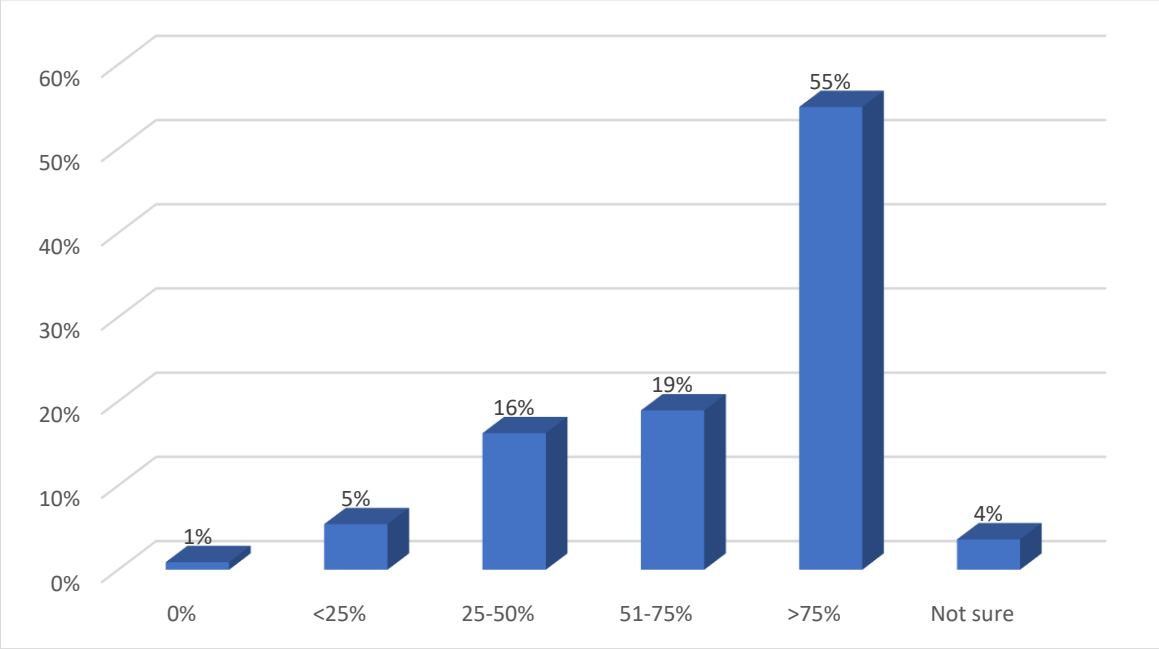
At what point would you order biomarker testing (beyond MSI) for a patient with unresectable or mCRC?



Forty-four percent of the oncologists surveyed reported that they would order biomarker testing (beyond MSI) for a patient with unresectable or mCRC after initial staging suggests

metastatic cancer, while others reported they would order biomarker testing at the time of initial biopsy (27%), upon initial diagnosis of CRC regardless of stage (14%), or if there is disease progression during or after initial therapy (10%). Other responses indicated that testing would be ordered upon the physician/oncologist's request.

What percentage of your patients with unresectable or mCRC undergo biomarker testing?



Who initiates the order(s) for biomarker testing for patients with unresectable or mCRC at your center? (Select all that apply)

Medical oncologist	69%
Pathologist	37%
Surgeon	18%
Nurse practitioner or physician assistant	5%
Oncology nurse	3%
Nurse navigator	1%
Not sure	2%

The majority of respondents (74%) reported that more than 50% of their patients with unresectable or mCRC undergo biomarker testing, whereas 22% of respondents reported that fewer than 50% of mCRC patients undergo biomarker testing. Medical oncologists most often order biomarker tests (69%), followed by pathologists (37%), surgeons (18%), and oncology advanced practitioners (5%).

On a scale from 1-5, with 1 being "not at all" and 5 being "extremely," how significant are the following factors in how you approach discussing biomarker testing with patients with unresectable or mCRC? (Select one for each item)

	Not at all significant 1	2	3	4	Extremely significant 5	Not sure
Patient's level of interest in being involved in decision-making	2%	7%	27%	30%	28%	6%
Patient's insurance status and coverage	3%	12%	25%	28%	24%	8%
Patient's family support	6%	10%	22%	34%	17%	11%
Patient's health literacy	6%	9%	23%	30%	23%	8%
Intention to enroll in a clinical trial(s)	4%	6%	19%	37%	29%	5%

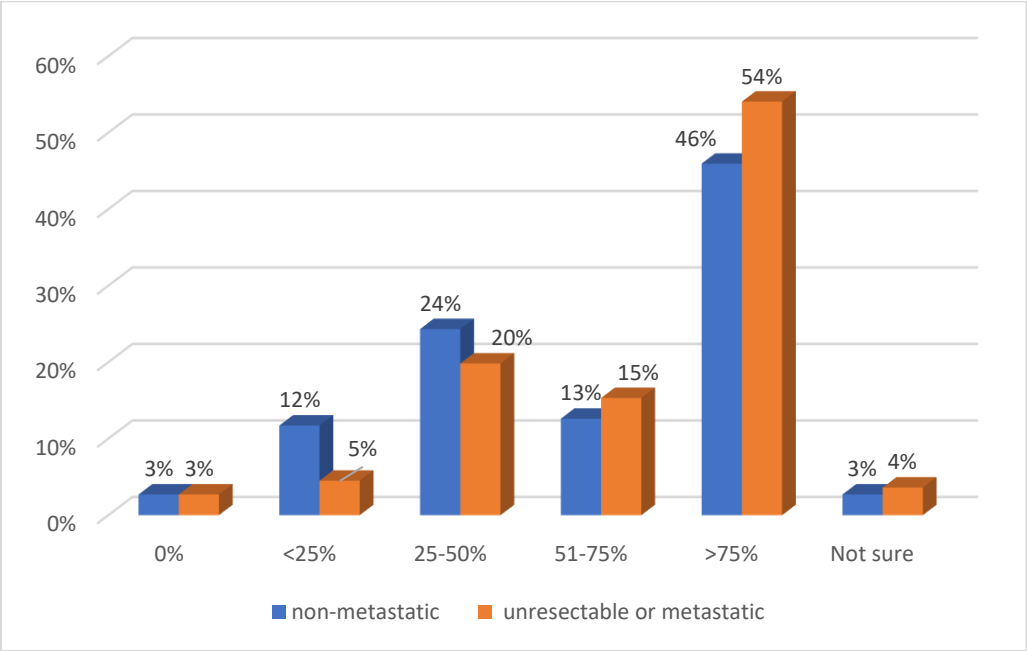
Among factors rated as significant (≥3) to practitioners' approach to discussing biomarker testing with patients, 85% of respondents indicated that both a patient's intent to enroll in a clinical trial and his or her level of interest in being involved in decision-making are equally important, followed by a patient's insurance status and coverage (77%), health literacy (76%), and level of family support (73%).

At your cancer practice, which biomarker test(s) are routinely ordered for patients with unresectable or mCRC at diagnosis? (Select all that apply)

KRAS mutation (exon 2) as a single test	28%
Extended KRAS mutations (exons 2, 3, and 4) as a single test	36%
NRAS mutation as a single test	35%
BRAF mutation as a single test	42%
HER2 amplification/overexpression as a single test	33%
Mismatch repair (MMR) / microsatellite instability testing (MSI)	56%
NTRK gene fusions	25%
Multiplex panel test that includes at least KRAS, NRAS, BRAF	41%
Large NGS panel test	33%
Liquid biopsy (e.g., Guardant360® CDx or Signatera)	20%
Not sure	4%

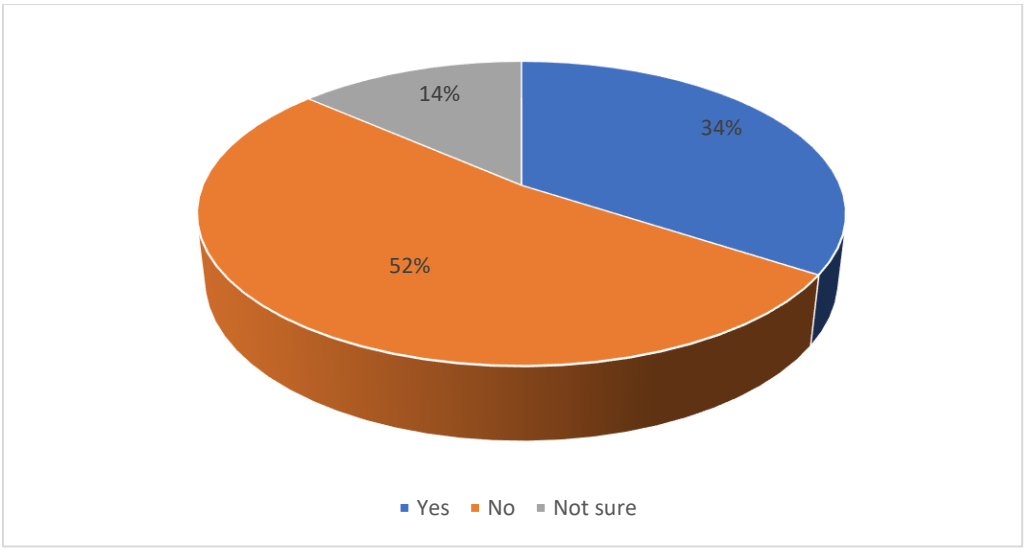
Most practitioners polled (56%) reported routinely ordering the MMR/MSI test for patients with unresectable or mCRC at diagnosis, while single biomarker tests such as BRAF mutation are routinely ordered by 42% of respondents, extended KRAS mutations (exons 2, 3, and 4) are ordered by 36%, NRAS mutation is ordered by 35%, HER2 amplification/overexpression is ordered by 33%, and KRAS mutation (exon 2 only) is ordered by 28%. Multiplex panel tests that include at least KRAS, NRAS, and BRAF are ordered by 41% of respondents, and large NGS panel tests are ordered by 33%. Twenty-five percent of respondents (25%) reported ordering NTRK gene fusions, and 20% ordered a liquid biopsy.

What percentage of your CRC patients with *non-metastatic disease* undergo dMMR/MSI testing? What percentage of your CRC patients with *unresectable or metastatic disease* undergo dMMR/MSI testing?



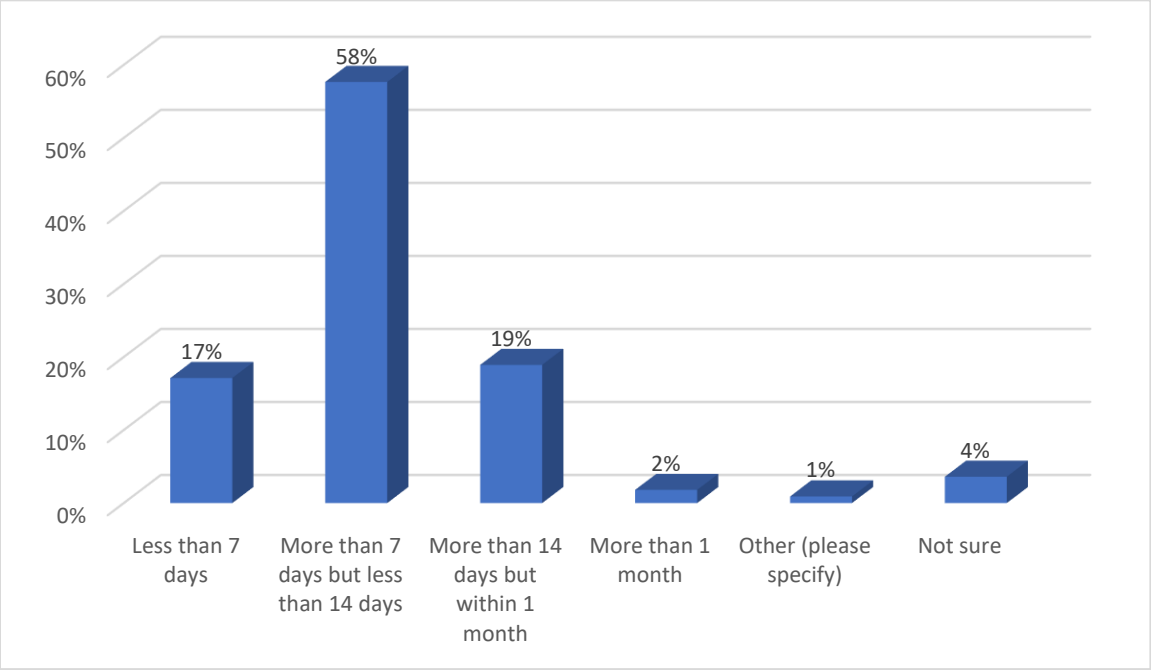
Fifty-nine percent of respondents (59%) reported that more than half of their patients with non-metastatic colorectal cancer undergo dMMR/MSI testing, while 69% reported that more than half of their patients with unresectable or mCRC undergo dMMR/MSI testing.

Does your cancer program have a standard protocol for unresectable or mCRC biomarker testing (e.g., standing orders or reflex biomarker testing according to a pathway)?



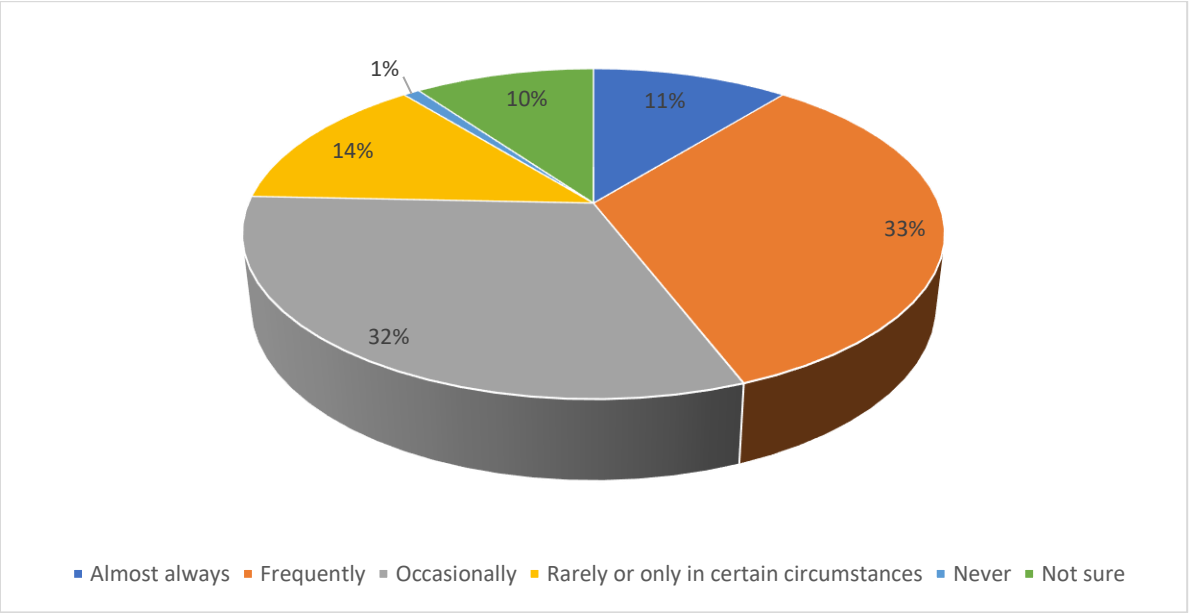
Fifty-two percent of respondents indicated that their cancer program has no standard protocol for biomarker testing for patients with unresectable or mCRC. Thirty-four percent of respondents indicated that they do have a standard protocol, and 14% were unsure.

Approximately how long does it take for you to receive complete testing results?



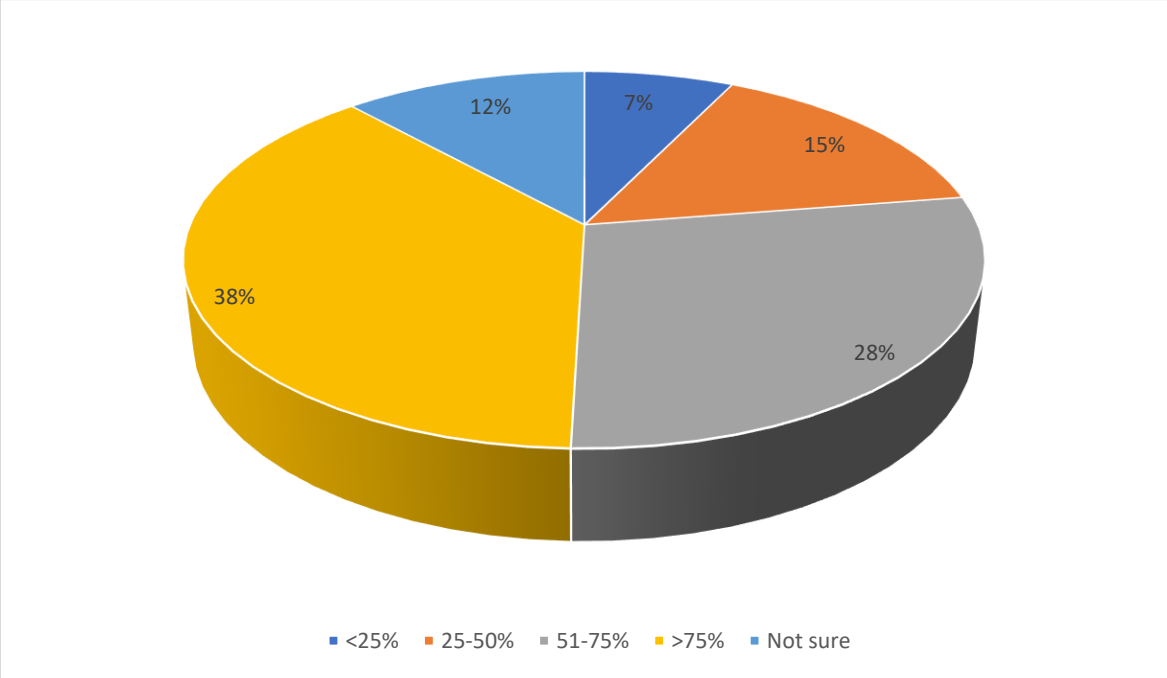
Among the centers that reported conducting biomarker testing, 58% reported a 1-2 week wait time to receive complete results, while 21% reported a wait time longer than 2 weeks. Only 17% of respondents reported a wait time of less than 1 week.

At your cancer program, how often are patients with unresectable or mCRC treated with systemic medical therapy before all biomarker test results are available?



For patients with unresectable or mCRC, treatment with systemic medical therapy before all biomarker test results are available was reported to occur “almost always” by 11% of respondents, “frequently” by 33%, “occasionally” by 32%, and “rarely or only in certain circumstances” by 14%. Only 1% of respondents reported that all biomarker test results are available before initiation of systemic medical therapy for their patients with unresectable or mCRC.

What percentage of your patients with unresectable or mCRC are treated based on their biomarker test results?



Among cancer centers caring for patients with unresectable or mCRC, 66% of respondents reported that more than half of patients receive treatment based on biomarker test results, while 22% reported that less than half of patients receive treatment based on biomarker test results.

On a scale from 1-5, with 1 being "not at all" and 5 being "extremely," how significant are each of the following <u>patient factors</u> in your approach to biomarker testing in a patient with unresectable or mCRC? (Select one for each item.)

	Not at all significant (1)	2	3	4	Extremely significant (5)	Not sure
Patient age	7%	9%	23%	32%	23%	6%
Gender	28%	15%	17%	21%	14%	5%
Race/ethnicity	30%	16%	22%	13%	14%	5%
Patient's general health/fitness	2%	6%	21%	40%	27%	5%
Patient's health literacy	8%	18%	24%	23%	21%	6%
Clinical trial eligibility	8%	7%	19%	33%	27%	5%
Patient preference	2%	7%	23%	37%	26%	5%
Insurance coverage	2%	12%	21%	36%	23%	6%
Presence of a caregiver	8%	14%	23%	36%	13%	6%

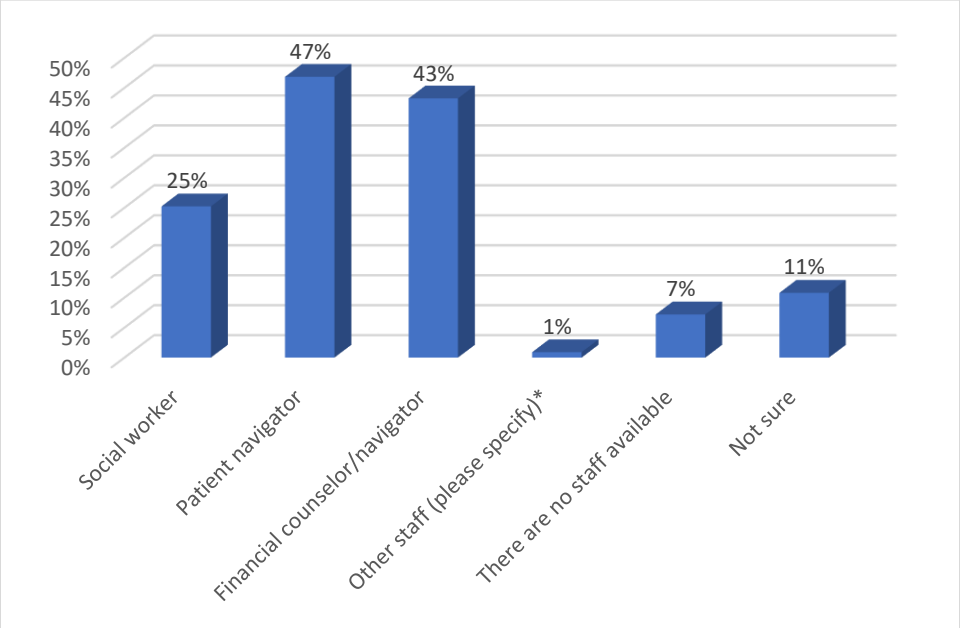
Among patient factors affecting practitioners' approach to biomarker testing in patients with unresectable or mCRC, a patient's general health and physical fitness was rated as significant (≥3) by 88% of those polled, followed by patient preference (86%), insurance coverage (80%), clinical trial eligibility (79%), and patient age (78%).

On a scale from 1-5, with 1 being "not at all" and 5 being "extremely," how significant are each of the following practice-level factors to the optimal use of biomarker testing in patients with unresectable or mCRC? (Select one for each item.)

	Not at all significant (1)	2	3	4	Extremely significant (5)	Not sure
Insufficient tissue for testing	1%	7%	25%	32%	32%	4%
Poor tissue quality	4%	5%	19%	37%	32%	4%
Long turn-around time	2%	13%	23%	34%	23%	5%
Lack of availability of in-house testing at my practice	14%	15%	24%	22%	22%	4%
Quality of in-house testing	14%	9%	21%	32%	20%	4%
Difficulty getting reimbursed	8%	16%	23%	29%	20%	5%
Patient refusal	14%	15%	15%	31%	18%	7%
Adequate staffing	17%	10%	26%	27%	13%	7%
Access to molecular tumor board	17%	12%	22%	30%	15%	5%
Familiarity with pathology report	16%	12%	20%	31%	19%	3%

When practice-level factors related to the optimal use of biomarker testing in patients with unresectable or mCRC were rated by survey participants, insufficient tissue for testing was rated as significant (≥3) by the greatest percentage of respondents (89%), followed by poor tissue quality (88%), long turn-around time (80%), patient refusal (74%), quality of in-house testing (73%), difficulty getting reimbursed (72%), lack of availability of in-house testing (68%), access to molecular tumor board (67%), and adequate staffing (66%).

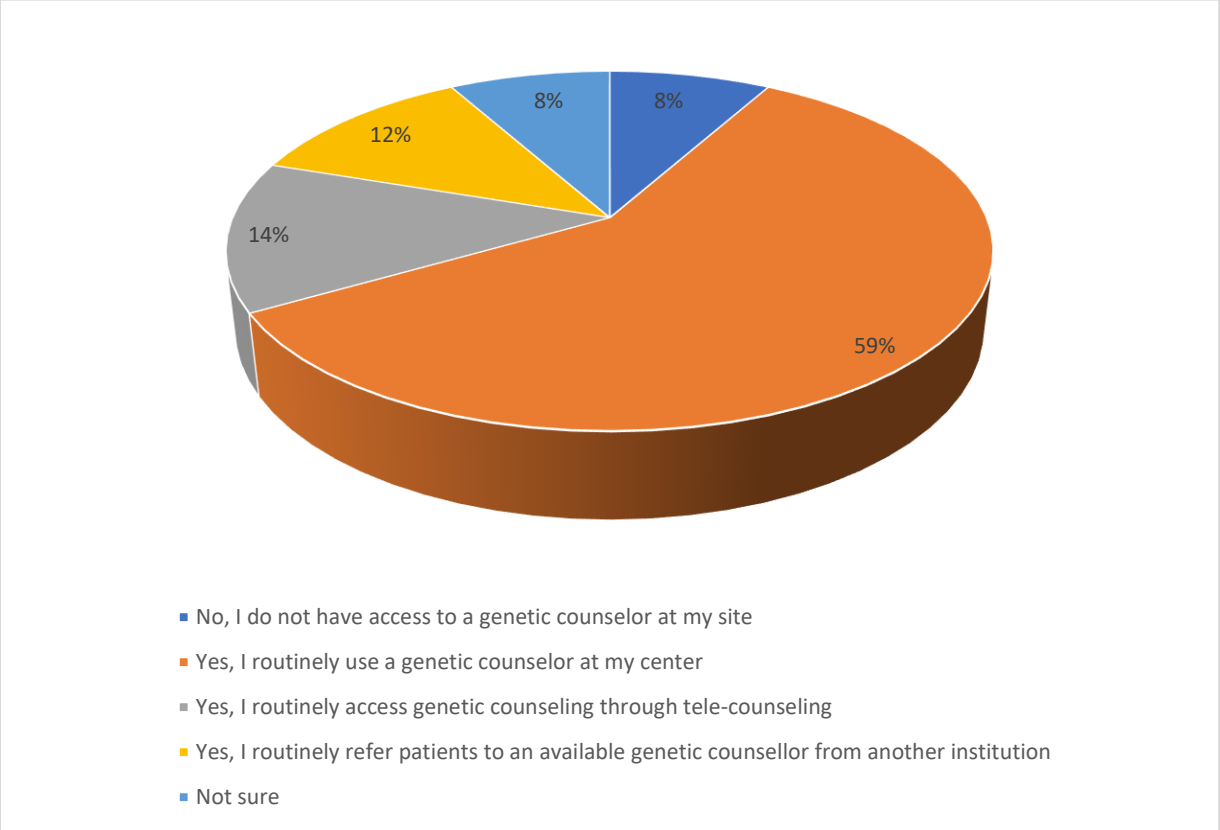
Who from your staff is available to answer patients' questions about costs/coverage related to biomarker testing? (Select all that apply)



Staff most commonly available to answer patients' questions related to the costs and coverage of biomarker testing include patient navigators (47%), financial counselors/navigators (43%), and social workers (25%).

*"Other staff" response: mid-level staff

Do you have access to, and routinely utilize, a genetic counselor?



While 8% of respondents reported no access to a genetic counselor, most centers reported using a genetic counselor either on site (59%) or via tele-counseling (14%). Twelve percent reported referring patients to the closest available genetic counselor at another institution.

At your center, who refers the patient for a genetic counseling appointment? (Select all that apply.)

Medical oncologist	81%
Surgeon	32%
Nurse practitioner or physician assistant	16%
Oncology nurse	15%
Nurse navigator	13%
Genetic counselor	11%
Nurse certified in genetics	4%
Self-referral	4%
Other (please specify)*	1%

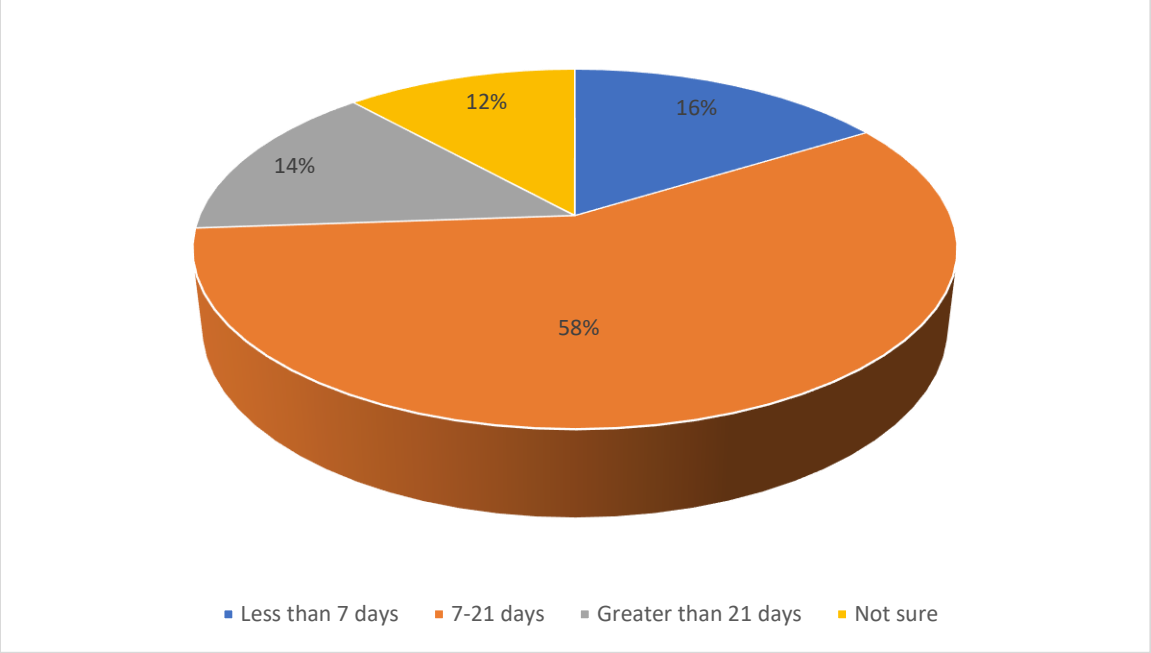
“Other” response: research coordinators

Who initiates the order for Lynch Syndrome testing at your center (select all that apply)?

Medical oncologist	68%
Surgeon	30%
Genetic counselor	23%
Nurse practitioner or physician assistant	16%
Oncology nurse	9%
Nurse navigator	6%
Nurse certified in genetics	1%
Other (please specify)	5%
Not sure	4%

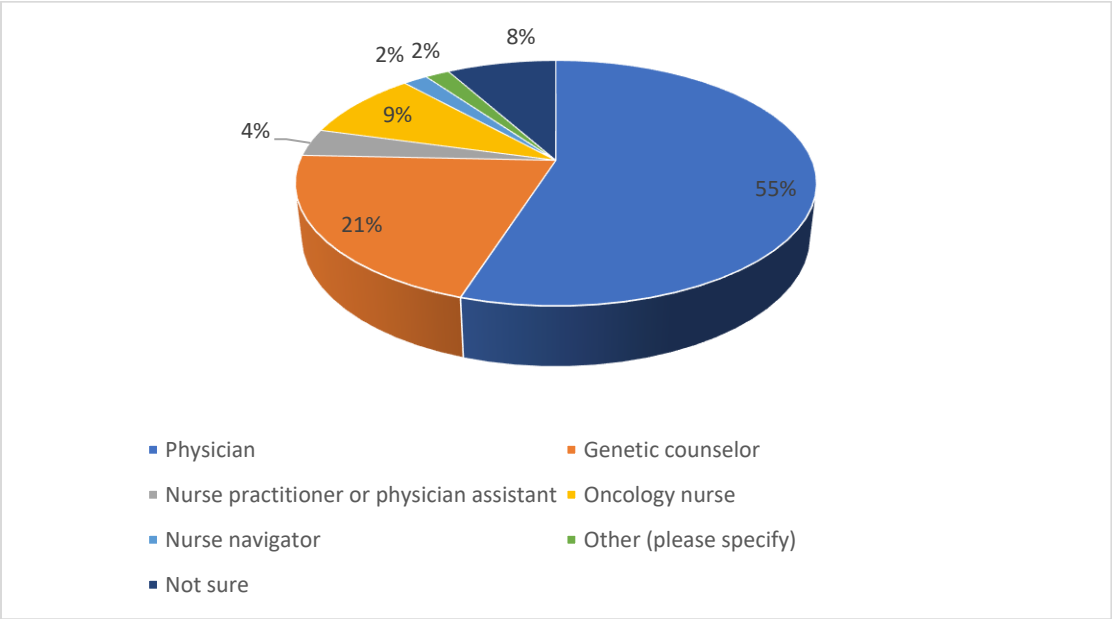
When available, genetic counseling consults are most often ordered by medical oncologists (81%), followed by surgeons (32%) and advanced practice providers (16%). When applicable, Lynch Syndrome testing is most often ordered by medical oncologists (68%), followed by surgeons (30%) and genetic counselors (23%).

What is the average time it takes to get a genetic counseling appointment?



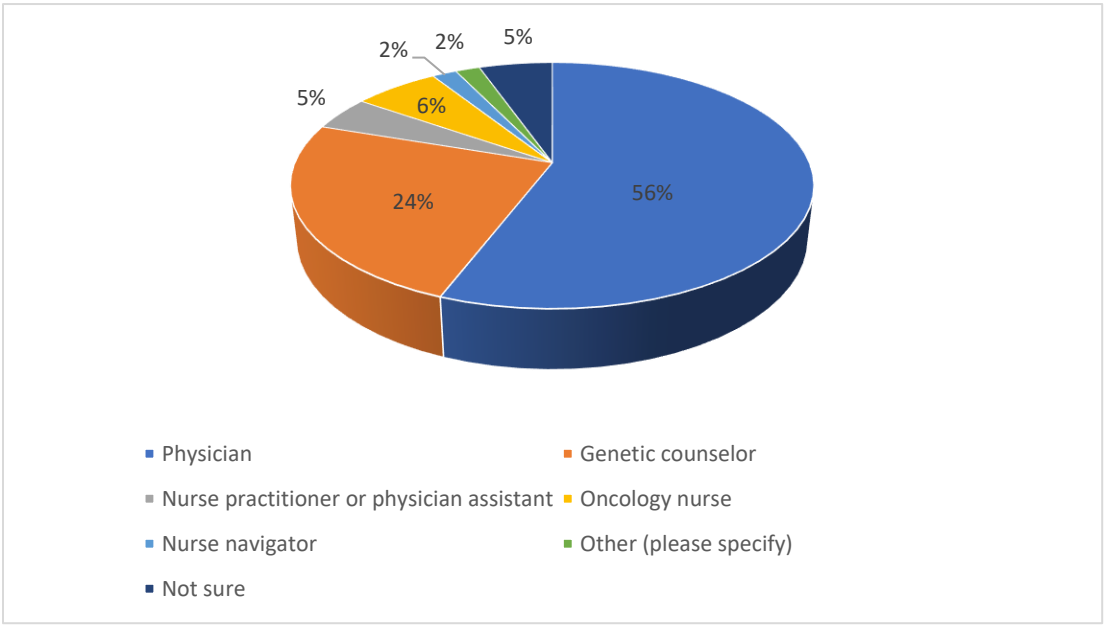
The majority of respondents (58%) indicated a 1-3 week wait time for a genetic counseling appointment, while others reported a wait time of longer than 3 weeks (14%). Only 16% of respondents reported a wait time of less than one week.

If you do not have access to a genetic counselor at your center, who educates patients about MSI and IHC testing for Lynch Syndrome *before* ordering the test?



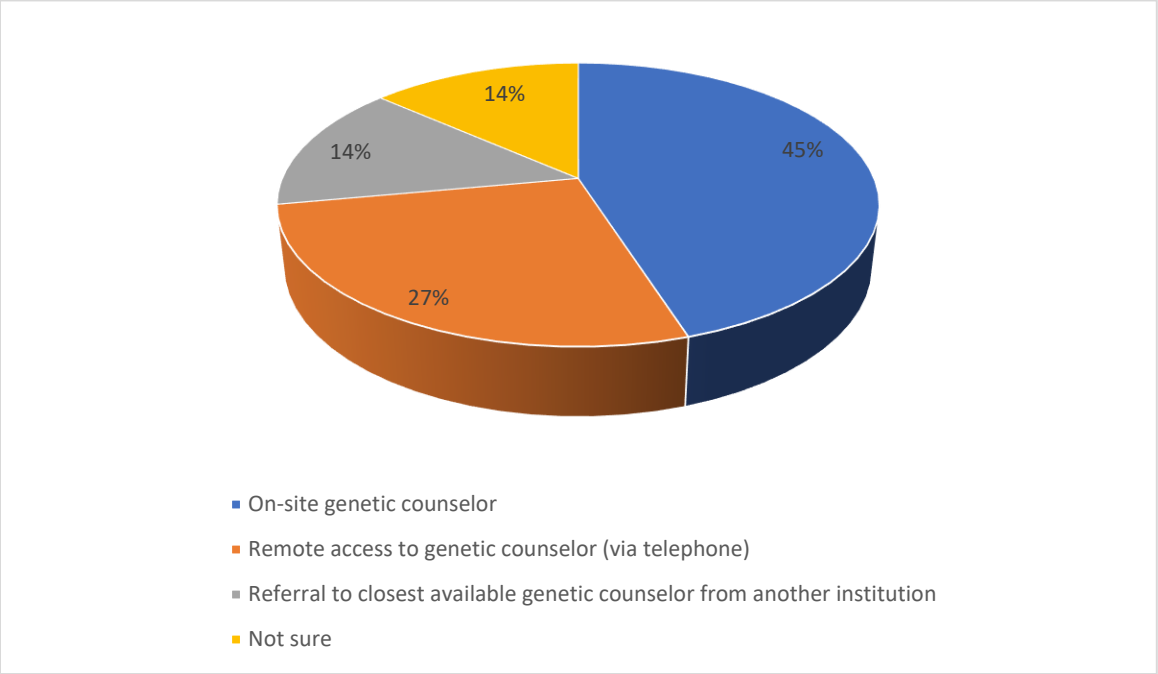
For cancer centers with no on-site access to genetic counseling, most of those surveyed (55%) reported that physicians provide patient education about MSI and IHC testing for Lynch Syndrome before ordering the test, followed by off-site or telehealth genetic counselors (21%), or oncology nurses (9%).

If you do not have access to a genetic counselor at your center, who educates patients about MSI and IHC testing for Lynch Syndrome *after* the test results are available?



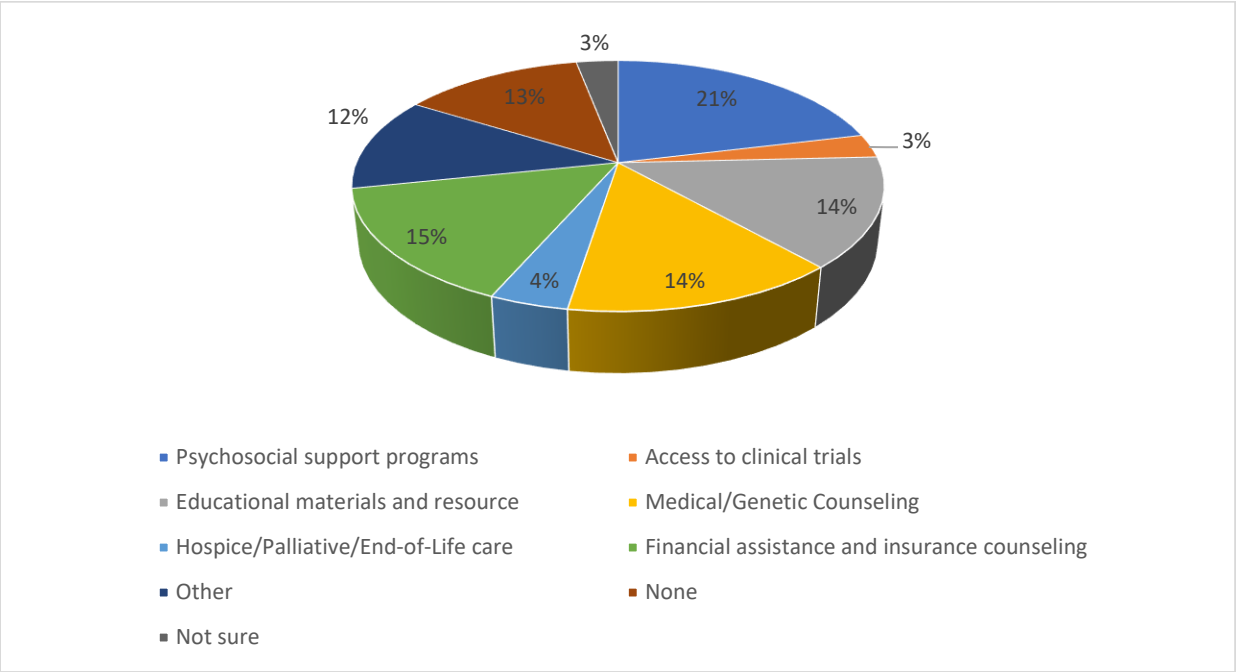
Cancer centers without on-site genetic counselors reported that patient education regarding the results of MSI and IHC testing for Lynch Syndrome was provided most often by physicians (56%), followed by off-site genetic counselors (24%).

How do you provide access to post-test genetic counseling at your site?



Among the cancer centers surveyed, 72% reported providing post-test genetic counseling either on site (45%) or through remote access to a genetic counselor via telephone (27%), while 14% of centers reported referring patients to a genetic counselor from another institution.

What resources do you feel your patients with unresectable or mCRC need most? (Please list all)



Summary

In a survey of community oncology practitioners conducted by ACCC to assess the status of biomarker testing in patients with unresectable or metastatic colorectal cancer (mCRC), more than 70% of respondents reported that more than half of their patients undergo biomarker testing. While 66% of respondents reported that more than half of their patients with unresectable or mCRC receive treatment based on biomarker test results, more than 40% reported that patients with mCRC who have had biomarker testing are treated with systemic medical therapy “frequently” or “almost always” before all biomarker test results are available.

Challenges to the optimal use of biomarker testing include both patient and practice factors. The patient factors most often cited as significant by survey respondents incorporate a wide range of circumstances, including a patient’s general health and physical fitness (88%), patient preference (86%), insurance coverage (80%), clinical trial eligibility (79%), and patient age (78%). The practice-level factors rated as significant by respondents include insufficient tissue for testing (89%), poor tissue quality (88%), long turnaround time (80%), patient refusal (74%), quality of in-house testing (73%), difficulty getting reimbursed (72%), and lack of availability of in-house testing (68%).

The majority of respondents indicated that they follow biomarker testing guidelines developed by NCCN (66%), followed by ASCO (45%) and a 2017 guideline jointly developed by the American Society for Clinical Pathology, College of American Pathologists, Association for

Molecular Pathology, and ASCO (32%). Fourteen percent said they employ a protocol developed by their institution or multidisciplinary team for ordering biomarker testing.

Most survey respondents (52%) indicated that their cancer program has no standard biomarker testing protocol for patients with unresectable or mCRC, such as standing orders or reflex biomarker testing according to a pathway. Among the biomarker tests routinely ordered at diagnosis of unresectable or mCRC, the MMR/MSI test was ordered by the greatest percentage of respondents (56%), followed by single gene mutation tests such as BRAF (42%), and multiplex panel tests including KRAS, NRAS, and BRAF (41%). Among the centers that reported conducting biomarker testing, 58% of respondents reported a 1-2 week wait time to receive complete results, with the highest percentage (47%) of respondents indicating that patient questions about costs and coverage related to biomarker testing are most commonly answered by patient navigators.

Among the practice variations identified by respondents in terms of access to and use of genetic counseling, 59% cited routinely using a genetic counselor, 14% cited using tele-counseling, 12% say they refer patients to the closest available genetic counselor at another institution, and 8% say they do not have access to a genetic counselor at their site. Genetic counseling appointments are typically arranged by medical oncologists (81%), as are tests for Lynch Syndrome (68%), with a 1-3 week wait time for genetic counseling appointments reported most often (58%). When asked what additional resources patients with unresectable or mCRC most need, practitioners most often listed psychosocial support programs, medical and genetic counseling, educational materials and resources, and financial assistance and insurance counseling.