Definitions of attributes included in the DCE instrument for patients and

physicians

Patient survey	Physician survey
Treatment Feature: Time Until Cancer	Treatment Feature: Progression-Free
Grows	Survival
One of the most important goals of cancer	No additional information provided
medicines is to keep the cancer from	
getting worse.	
Later in the survey we will ask you	
to think about how long the	
medicine can keep the cancer	
from growing or getting worse.	
The medicine may help for a	
while, but it may stop working at	
some point and then the cancer	
will grow again.	
Treatment Feature: Chance of Severe	Treatment Feature: Chance of Severe
Skin Rash	Papulopustular Rash
Some medicines for mCRC may cause a	Some medications for colorectal cancer
skin reaction that will result in a severe	may cause a severe papulopustular rash.
rash.	Symptoms of a severe papulopustular
A severe skin rash is an outbreak of at	rash typically appear within the first 2
least 20 red solid bumps or blisters on the	

face, upper back or chest. A severe rash can also be diagnosed when having more than five areas around the body that have skin redness with swelling, each covering about the size of a dime.

With severe rashes, a person will have more than one third of the body with scaly skin that itches, cracks and peels, resulting in serious infections that need to be treated with medicines. A person with a severe rash will also have areas of redness that are painful and cover more than one third of the body.

Itching is constant and affects the person's ability to sleep.

Finally, a person with a severe skin rash will have problems doing some daily activities, like:

- o Bathing
- o Dressing and undressing
- o Eating

The rash typically begins within the first 2 weeks of taking a medicine and lasts for up to a month. weeks of taking the medication and last for up to a month.

A patient with a severe papulopustular rash will have more than 20 papules or pustules; or more than 5 areas of erythema/edema that are less than 1cm in size. These papules or pustules may include pain and pruritus. With a severe papulopustular rash, the patient will experience painful erythema covering more than 30% of the body. They will also experience severe, widespread, and constant pruritus interfering with sleep. Scaling and flaking on the skin will cover more than 30% of the body causing fissuring and cracking that lead to signs of super infection. A patient with a severe papulopustular rash will experience limitations in activities of daily life, such as bathing, dressing and undressing, and feeding him or herself.

Treatment Feature: Chance of Serious
Hemorrhage
Some medications for colorectal cancer
may cause serious hemorrhages. Serious
hemorrhages include:
Bleeding in large quantities (causing a
drop in hemoglobin of at least 2 g/dl
and/or leading to a transfusion of 2 or
more units of packed red blood cells or
whole blood), or
Bleeding in a critical site (subdural,
subarachnoid, epidural, intraspinal,
intraocular, pericardial, intra-articular,
intramuscular with compartment
syndrome, or retroperitoneal).
Treatment Feature: Chance of GI
perforations
No additional information provided

Inflammation of pouches	
(diverticulitis) or ulcers in the	
intestine wall	
A recent sigmoidoscopy or	
colonoscopy (a test that inserts a	
flexible tube through the rectum to	
check the large and small	
intestine)	
 Having part of a tumor in the GI 	
tract removed	
 Exposure to radiation to treat a 	
tumor in the past	
 Blockage of the intestine 	
 Multiple previous surgeries in the 	
GI tract	
With GI perforations you can feel stomach	
pain, chills, fever, nausea, and vomiting.	
GI perforations need to be treated	
immediately. Treatment usually involves	
surgery to repair the hole. The majority of	
patients recover completely after surgery.	
Treatment Feature: Chance of a Severe	Treatment Feature: Chance of
Heart Attack	cardiopulmonary arrest
Some medicines for mCRC may cause a	No additional information provided
severe heart attack. A severe heart attack	

Supplement: Patient Survey

Metastatic Colorectal Cancer Treatment Preferences

Thank you for your interest in this medical survey. In this survey, we will ask you about your experience with metastatic colorectal cancer. You have metastatic colorectal cancer (mCRC) when you have or had a tumor in your colon or rectum that has spread to other parts of the body, such as the liver, lymph nodes, lungs, or bones. We will ask you what you think about the features of different medicines used to treat mCRC.

If you have any problems or concerns about this survey, please email Ms. Valerie Tower at <u>vtower@rti.org</u> at the Research Triangle Institute.

Please answer the following questions to confirm that you are eligible to participate in this survey.

- S1. Are you 18 years of age or older?
 - Yes [Continue]
 - No [Ineligible, end survey]
- S2. Have you been told by a doctor that you have or had colorectal cancer that has spread to other parts of your body?
 - Yes [Continue]
 - No [Ineligible, end survey]

[Eligible if answer YES to S1, and S2.]

[If ineligible, end survey.]

Study Purpose

You are one of about 300 people with mCRC in the United States who are being asked to take a survey to help us understand people's preferences for different medicines to mCRC. In this survey we will ask you about your experience with mCRC and your thoughts about possible medicines to mCRC.

Study Duration

The survey will take about 25 minutes to complete.

Study Details

This research study is being run by Research Triangle Institute (RTI) on behalf of a pharmaceutical company. RTI is a not-for-profit research organization in Research Triangle Park, North Carolina, United States. RTI has contracted with Nielsen to collect data. If you have questions about this survey, please send an e-mail to RTI investigators at <u>vtower@rti.org</u>. Messages will be answered within 24 hours of their receipt.

Possible Risks or Discomforts

If any questions make you uncomfortable, you do not need to answer them.

AllPoints will protect your responses under its Privacy Policy. RTI and the pharmaceutical company will receive your survey responses, no personal identifiers. RTI also will make every effort to protect your responses. There is a potential risk of disclosure of the survey data, but the data could not be directly tied to you.

If you have concerns about your rights as a participant, you may e-mail the RTI Office of Research Protection at <u>ORPE@rti.org</u>.

Benefits

There are no direct benefits to you from participating in this study. Your responses are very important because they will help researchers to understand people's preferences for different medicines to treat mCRC.

Confidentiality

Many steps have been taken to protect your information. AllPoints will report only your responses to RTI, not your names. If the results of this study are presented at scientific meetings or published in scientific journals, no information will be included that could identify you or your responses personally.

The Institutional Review Board (IRB) at RTI has reviewed this research. An IRB is a group of people who make sure that the rights of participants in research are protected. The IRB may check records of your activity in this research to see if proper procedures were followed.

Your Rights

Your decision to take part in this research study is completely voluntary. Your decision to participate in this study will not affect your usual medical care. You can refuse to answer any question or stop at any point after you begin the survey.

If you have read the previous screens and agree to participate, please click the Yes button, if not, click the No button.



- Yes, I agree to participate. [continue with next section]
- No, I do not agree to participate. [go on to next question]

Are you sure you don't want to participate? Your opinions are important to us. Please select the Yes button to continue this survey; if not, select the No button to exit.



- Yes, I agree to participate. [continue with next section]
- No, I <u>do not agree</u> to participate [end survey].

[If they do not agree to participate]

Thank you for your time. You have exited the survey.

Tell us about yourself

B1. What is your gender?

Male

Female

B2. What year were you born? _____

B3. What is your marital status?

Single /	never	married
-		

Married / living as married / civil partnership

Divorced or separated

Widowed / surviving partner

Other

Γ

L

B4.	What is the highest level of education you have completed?
	(Check only one answer.)

	Less than high school
	Some high school
	High school or equivalent (e.g., GED)
	Some college but no degree
	Technical school
	Associate's degree (2-year college degree)
	4-year college degree (e.g., BA, BS)
	Some graduate school but no degree
	Graduate or professional degree (e.g., MBA, MS, MD, PhD)
B5.	Which of the following <u>best</u> describes your employment status? (Check only one answer.)
	Employed
	Self-employed

Student

Retired

Unemployed

Disabled/Unable to work

Γ

Your Experience with Metastatic Colorectal Cancer (mCRC)

1. How long ago did a doctor tell you that your colorectal cancer had spread to other parts of your body?

	Less	than s	six month	ns ago	
_	7				

At least six months ago, but less than one year ago

At least one year ago, but less than two years ago

At least two years ago	but less than	five years ago
------------------------	---------------	----------------

- At least five years ago
- 2. To which parts of your body has your doctor said cancer has spread? (Check all that apply.)

Lymph nodes	[Go to question 3]
-------------	-------------------	---

Liver [Skip to question 5 if "Lymph nodes" was not chosen]

Lungs [Skip to question 5 if "Lymph nodes" was not chosen]

Bones [Skip to question 5 if "Lymph nodes" was not chosen]

- Inner lining of the abdomen (peritoneum) [Skip to question 5 if "Lymph nodes" was not chosen]
- Uterus [Skip to question 5 if "Lymph nodes" was not chosen]
- Esophagus [Skip to question 5 if "Lymph nodes" was not chosen]
- Other [Skip to question 5 if "Lymph nodes" was not chosen]

3. To which lymph nodes did your cancer spread? (Check all that apply.)

4.

5.

Head and neck
Chest
Abdomen
Arms and legs
Other
Did your doctor remove lymph nodes to which the cancer had spread?
Yes
No
Don't know
Which symptoms of mCRC have you experienced? (Check all that apply.)
Gas, cramps, feeling full
Blood in your stool or very dark stools
Changes in your bowels such as more frequent stools, thinner stools, or feeling that your bowels are not fully emptying
Pain Pain
Loss of appetite
Weight loss
Eeling tired
Problems with memory, concentration, balance or movement
None of the above
Other

6. Has your doctor ever given you a genetic test to see if your cancer has the KRAS gene mutation?

Yes

No [Skip to Question 8]

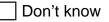
Don't know [Skip to Question 8]

IF Q6 = YES, ASK:

7. Which type of the KRAS gene does your cancer have?

KRAS wild-type (or normal)

KRAS mutation



8. Which of the following options best describes your mCRC treatment?



I am currently being treated

I am not currently being treated, but had treatment in the past [Skip to question 12]

I have not had treatment for mCRC [Skip to FEATURES OF TREATMENTS]

IF Q8 = CURRENT OR PAST, ASK:

9. Which side effects of treatments for mCRC have you experienced? (Check all that apply.)

Nausea	or	vomiting

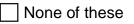
Depression

Pain

Г	all	1	

Sexual problems	5
-----------------	---

Other



10. How are you currently being treated for mCRC? (Check all that apply.)

Pills or tablets [Skip to question 12]

Intravenous (IV) medicine (at a doctor's office, hospital, or clinic)

Routine check-ups [Skip to question 12]

Don't know [Skip to question 12]

Other [Skip to question 12]	
-----------------------------	--

11. Do you have a port (a small device that is implanted under your skin to allow easy access to your bloodstream) that is used to administer your IV medicine?

	Yes
--	-----

Nc

Don't know

12. Which of the following describes how you have <u>ever</u> received treatment for mCRC? *(Check all that apply.)*

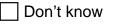
] Pills or tablets

Intravenous (IV) medicine (at a doctor's office, hospital, or clinic) <u>not through</u> a port device (a small device that is implanted under your skin to allow easy access to your bloodstream)

Intravenous (IV) medicine (at a doctor's office, hospital, or clinic) <u>through</u> a port device (a small device that is implanted under your skin to allow easy access to your bloodstream)

Routine check-up	s
------------------	---

Radiation



	Other
--	-------

Features of Treatments for Metastatic Colorectal Cancer

Medicines for mCRC can help people live longer and keep symptoms from getting worse.

Later in this survey, we will ask you to think about hypothetical medicines doctors may prescribe in addition to chemotherapy to help treat mCRC. In the next few pages, we will describe features of mCRC medicines. If needed, you can refer to this information as you take the survey.

Treatment Feature: Time Until Cancer Grows

One of the most important goals of cancer medicines is to keep the cancer from getting worse.

Later in the survey we will ask you to think about how long the medicine can keep the cancer from growing or getting worse. The medicine may help for a while, but it may stop working at some point and then the cancer will grow again.

Thinking about the chance of getting a side effect

Some medicines for mCRC have a chance of side effects. Later in this survey, we will ask you to consider medicines with different chances of getting different side effects. The following pictures may help you think about how many people might get a side effect.

Every figure in the pictures below represents 1 person who is taking a mCRC medicine. There are 100 figures in the picture. The figures shown in color indicate people who <u>will get</u> a side effect while taking a mCRC medicine. The figures shown in gray indicate the number of people who <u>will not get</u> a side effect while taking a mCRC medicine. The number of people who will get a side effect tells you how big is the chance of getting the side effect.

<u>Ħ</u>ĦŔŔŔŔŔŔŔŔŔŔŔŔŔŔŔŔŔŔŔŔ

In this example:

10 of the figures are shown in color. That means that 10 people out of 100 (10%) <u>will</u> get a side effect while taking a mCRC medicine.

90 of the figures are shown in gray. That means that 90 people out of 100 (90%) <u>will not</u> get a side effect while taking a mCRC medicine.

In this example:

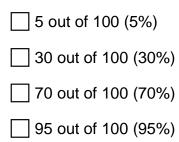
25 of the figures are shown in color. That means that 25 people out of 100 (25%) <u>will</u> get a side effect while taking a mCRC medicine.

75 of the figures are shown in gray. That means that 75 people out of 100 (75%) <u>will not</u> get a side effect while taking a mCRC medicine.

Please look at the picture to the right:



13. If each figure in the picture is 1 person who takes a medicine to treat his or her mCRC, how many people who take the medicine will get a side effect?



[if Q13 is not "30%"]

Please look at the picture to the right:



You said that [response to Q13] people would have a side effect. Given your response, we would like to remind you that the figures shown in color represent people who will have a side effect.

In the picture above there are 100 figures. Only 30 of them are shown in color, while the rest are shown in gray. This means that 30 out of 100 (or 30%)people who take a medicine will get a side effect. The correct answer is 30 out of 100 (30%).

Treatment Feature: Chance of Severe Skin Rash

Some medicines for mCRC may cause a skin reaction that will result in a severe rash.

A severe skin rash is an outbreak of at least 20 red solid bumps or blisters on the face, upper back or chest. A severe rash can also be diagnosed when having more than five areas around the body that have skin redness with swelling, each covering about the size of a dime.

With severe rashes, a person will have more than one third of the body with scaly skin that itches, cracks and peels, resulting in serious infections that need to be treated with medicines. A person with a severe rash will also have areas of redness that are painful and cover more than one third of the body.

Itching is constant and affects the person's ability to sleep.

Finally, a person with a severe skin rash will have problems doing some daily activities, like:

- o Bathing
- Dressing and undressing
- o Eating

The rash typically begins within the first 2 weeks of taking a medicine and lasts for up to a month.

14. Have you ever experienced a severe skin rash?

Yes

No [Skip to question 17]

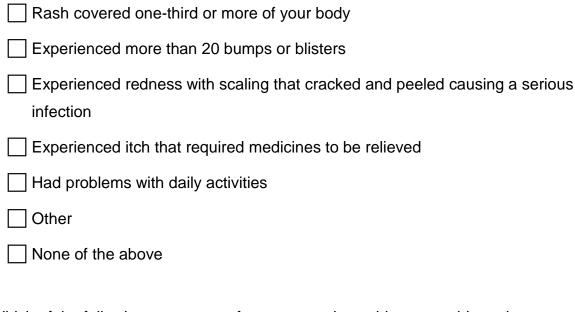
15. Do you know of anyone who has had a severe skin rash?

Yes
N 1

_ No

Don't know

16. Which of the following symptoms did you	experience the last time you had a severe
rash? (Check all that apply)	



17. Which of the following symptoms of a severe rash would you consider to be most concerning?

Have the rash cover one-third or more of your body

Experience more than 20 bumps or blisters

Experience redness with scaling that cracks and peels causing a serious infection



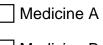
Have problems with daily activities

Thinking about treatments for mCRC

Imagine that a person was recently diagnosed with mCRC. The doctor tells this person that they need to start a new medicine for mCRC immediately. There are two possible hypothetical medicines that this person can take to treat mCRC.

Hypothetical Medicine A cancer from getting wors next 12 months, but will chance of causing seven	se for the have a 20%	cancer f	etical Medicine B will keep from getting worse for the months, but will have a 5% of causing severe skin rash.
Medicine Feature	Medicine A		Medicine B
How long before the cancer grows	12 months		24 months
Chance of severe skin rash	20% (20 out of 100)		5% (5 out of 100)

18. Which medicine will keep cancer from growing for a longer period of time?



] Medicine B

Medicine Feature	Medicine A	Medicine B
How long before the cancer grows	12 months	24 months
Chance of severe skin rash	20% (20 out of 100)	5% (5 out of 100)

Q RAMP UP 1. If you were the person taking the medicine, which hypothetical medicine would you choose?

Medicine A

] Medicine B

Treatment Feature: Chance of Serious Bleeding Events

Some medicines for mCRC can cause serious bleeding events. In a serious bleeding event, a person has a large amount of bleeding or bleeds in a critical area of their body such as the head, spine, near the heart, in the abdomen, or in the joints. People may feel weak and tired and feel a lot of pain.

Most people who experience serious bleeding events will need to be admitted to the hospital and have a blood transfusion or surgery.

20. Have you ever experienced a serious bleeding event?

	Yes
--	-----

No [Skip to THINKING ABOUT TREATMENTS]

Don't know [Skip to THINKING ABOUT TREATMENTS]

21. Where in your body was your serious bleeding event?

Head	
Spine Spine	
Near the heart	
Abdomen	
Joints	
Other	

Thinking about treatments for mCRC

Again, imagine that a person was recently diagnosed with mCRC. The doctor tells this person that they need to start a new medicine for mCRC immediately. There are two possible medicines this person can take to treat mCRC.

Q RAMP UP 2

Medicine Feature	Medicine A	Medicine B
How long before the cancer grows	12 months	24 months
Chance of severe skin rash	20% (20 out of 100)	5% (5 out of 100)
Chance of serious bleeding events	10% (10 out of 100)	1% (1 out of 100)
If you were taking the medicine, which medicine would you choose?		

Treatment Feature: Chance of Gastrointestinal (GI) Perforations

Some mCRC medicines may cause gastrointestinal (GI) perforations. GI perforations are holes that develop anywhere in the GI tract, which includes your stomach, intestines, and colon.

GI perforations are more common in patients who have had problems with their GI tract in the past, such as:

- Inflammation of pouches (diverticulitis) or ulcers in the intestine wall
- A recent sigmoidoscopy or colonoscopy (a test that inserts a flexible tube through the rectum to check the large and small intestine)
- Having part of a tumor in the GI tract removed
- Exposure to radiation to treat a tumor in the past
- Blockage of the intestine
- Multiple previous surgeries in the GI tract

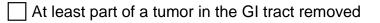
With GI perforations you can feel stomach pain, chills, fever, nausea, and vomiting. GI perforations need to be treated immediately. Treatment usually involves surgery to repair the hole. The majority of patients recover completely after surgery.

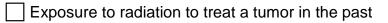
22. Which of the following have you had?	(Check all that apply.)
--	-------------------------

\square	Pouches	(diverticulitis)	or ulcers in	n the	intestine	wall
-----------	---------	------------------	--------------	-------	-----------	------

A recent sigmoidoscopy

A recent	colonoscopy
----------	-------------





- Blockage of the intestine
- Multiple previous surgeries in the GI tract
- None of the above

23. Have you ever had a GI perforation?

Yes
No

Don't know

24. Do you know someone who has had a GI perforation?

_ Yes _ No

Treatment Feature: Chance of a Severe Heart Attack

Some medicines for mCRC may cause a severe heart attack. A severe heart attack occurs when the heart stops beating normally and blood does not flow like it should. Without blood flow, the body does not get the oxygen it needs. During a severe heart attack people may lose their breath and pass out. Without medical help, a person having a severe heart attack could die within a few minutes.

Even if a person survives a severe heart attack, their heart will be weaker after the heart attack. With a weaker heart, a person will get tired more quickly and have shortness of breath when doing normal daily activities.

25. Have you ever had a heart attack?

Yes
No

26. Do you know someone who has died of a heart attack?

Yes
No

27

Your opinions about medicines for metastatic colorectal cancer

Again, imagine that a person was recently diagnosed with mCRC. The doctor tells this person that they need to start a new medicine for mCRC immediately.

In the next [INSERT # BASED ON EXPERIMENTAL DESIGN] questions, we will show you different pairs of hypothetical medicines that this person could take to treat mCRC. For each pair, please tell us which medicine you would choose (Medicine A or Medicine B) if you had to make this decision for yourself.

If you need to see the description for any treatment feature, please refer to the descriptions provided earlier in this survey.

Please assume that any medicine costs, including those related to treating or managing side effects, are fully covered by insurance.

Even if you don't think either medicine is very good, please choose the one that you think would be best if you had no other options. Please choose based on how you personally feel about the medicines shown. There are no right or wrong answers.

[Example question] – WILL BE BASED ON EXPERIMENTAL DESIGN AND WILL BE USED TO ESTIMATE PREFERENCE WEIGHTS

Choice Question 1

Medicine Feature	Medicine A	Medicine B
How long before the cancer grows	12 months	8 months
Chance of severe skin rash		20% (20 out of 100)
Chance of serious bleeding	1% (1 out of 100)	10% (10 out of 100)
Chance of GI perforations	2% (2 out of 100)	1% (1 out of 100)
Chance of a severe heart attack	None	
If you were taking the medicine, which medicine would you choose?		

[Final set of choice questions will be determined based on an experimental design]

FOLLOW-UP QUESTIONS ARE STATIC, NOT PART OF THE EXP. DESIGN IN CHOICE QUESTIONS

FOLLOW UP 1

Suppose your doctor presented to you the following options today.

- You could delay cancer growth for 6 months and expect to live for 36 months
- You could delay cancer growth for 12 months and expect to live for 24 months

Medicine Feature	Medicine A	Medicine B	
Length of life	36 months 24 months		
How long before the cancer grows	6 months	12 months	
Chance of severe skin rash	None	None	
Chance of serious bleeding	None	None	
Chance of GI perforations	None	None	
Chance of a severe heart attack	None	None	
If you were taking the medicine, which	[Go to FOLLOW UP 2]	[Go to FOLLOW UP 3]	

medicine would you	
choose?	

FOLLOW UP 2

Suppose your doctor presented to you the following options today.

- You could delay cancer growth for 6 months and expect to live for 28 months
- You could delay cancer growth for 12 months and expect to live for 24 months

Medicine Feature	Medicine A	Medicine B
Length of life	28 months	24 months
How long before the cancer grows	6 months	12 months
Chance of severe skin rash	None	None
Chance of serious bleeding	None	None
Chance of GI perforations	None	None
Chance of a severe heart attack	None	None
If you were taking the medicine, which medicine would you choose?		

GO TO Q27 INTRO

FOLLOW UP 3

Suppose your doctor presented to you the following options today.

- You could delay cancer growth for 6 months and expect to live for 36 months
- You could delay cancer growth for 12 months and expect to live for 20 months

Medicine Feature	Medicine A	Medicine B
Length of life	36 months	20 months
How long before the cancer grows	6 months	12 months
Chance of severe skin rash	None	None
Chance of serious bleeding	None	None
Chance of GI perforations	None	None
Chance of a severe heart attack	None	None
If you were taking the medicine, which medicine would you choose?		

Q27 INTRO

Suppose your doctor presented to you the following options today.

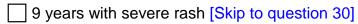
27. Would you rather live 10 years with severe rash or 7 years in perfect health?

10 years with severe rash



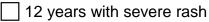
7 years in perfect health [Skip to question 29]

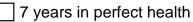
28. Would you rather live 9 years with severe rash or 7 years in perfect health?



7 years in perfect health [Skip to question 30]

29. Would you rather live 12 years with severe rash or 7 years in perfect health?





Suppose you were presented with the following options today.

Q30, 31, 32 – SHOW RESPONDENT 2% OR 5% OR 9% CONSISTENTLY ACROSS THESE 3 QUESTIONS:

30. Would you rather live 10 years with a [randomize across respondents: 2%; 5%; 99	%]
chance each year of <u>serious bleeding events</u> or 7 years in perfect health?	

] 10 years with a [randomize across respondents: 2%; 5%; 9%] chance each year of serious bleeding events

7 years in perfect health [Skip to question 32]

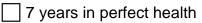
31. Would you rather live 9 years with a [randomize across respondents: 2%; 5%; 9%] chance each year of <u>serious bleeding events</u> or 7 years in perfect health?

9 years with a [randomize across respondents: 2%; 5%; 9%] chance each year of serious bleeding events [Skip to question 33]

7 years in perfect health [Skip to question 33]

32. Would you rather live 12 years with a [randomize across respondents: 2%; 5%; 9%] chance each year of <u>serious bleeding events</u> or 7 years in perfect health?

12 years with a [randomize across respondents: 2%; 5%; 9%] chance each year of serious bleeding events

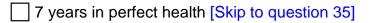


Q33, 34, 35 – SHOW RESPONDENT 2% OR 5% OR 9% CONSISTENTLY ACROSS THESE 3 QUESTIONS:

Suppose you were presented with the following options today.

33. Would you rather live 10 years with a [randomize across respondents: 2%; 5%; 9%] chance each year of <u>GI perforations</u> or 7 years in perfect health?

10 years with [randomize across respondents: 2%; 5%; 9%] chance each year of GI perforations



34. Would you rather live 9 years with a [randomize across respondents: 2%; 5%; 9%] chance each year of <u>GI perforations</u> or 7 years in perfect health?

9 years with [randomize across respondents: 2%; 5%; 9%] chance each year of GI perforations [Skip to question 36]

7 years in perfect health [Skip to question 36]

35. Would you rather live 12 years with a [randomize across respondents: 2%; 5%; 9%] chance each year of <u>GI perforations</u> or 7 years in perfect health?

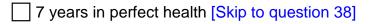
] 12 years with [randomize across respondents: 2%; 5%; 9%] chance each year of GI perforations

Q36, 37, 38 – SHOW RESPONDENT 2% OR 5% OR 9% CONSISTENTLY ACROSS THESE 3 QUESTIONS:

Suppose you were presented with the following options today.

36. Would you rather live 10 years with a [randomize across respondents: 2%; 5%; 9%] chance each year of a severe heart attack or 7 years in perfect health?

10 years with a [randomize across respondents: 2%; 5%; 9%] chance each year of a severe heart attack



37. Would you rather live 9 years with a [randomize across respondents: 2%; 5%; 9%] chance each year of a <u>severe heart attack</u> or 7 years in perfect health?

] 9 years with a [randomize across respondents: 2%; 5%; 9%] chance each year of a severe heart attack [Skip to question 39]

7 years in perfect health [Skip to question 39]

38. Would you rather live 12 years with a [randomize across respondents: 2%; 5%; 9%] chance each year of a severe heart attack or 7 years in perfect health?

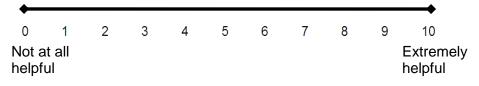
] 12 years with a [randomize across respondents: 2%; 5%; 9%] chance each year of a severe heart attack

39. How did you learn about the side effects of your mCRC treatment? (Check all that apply.)

Doctor
Nurses
Physician's assistant
Other staff at your doctor's office
Example or friends
Books, magazines, pamphlets, or journals
Internet (such as medical websites or group forums)
Other

40. On the scale from 0 to 10, please select the number that best describes how helpful the information was about the potential side effects of your mCRC treatment?

INCLUDE NUMBERS AND RADIO BUTTONS



41. With which of the following medical conditions have you been diagnosed?

(Check all that apply.)

Arthritis
Asthma or allergies
Diabetes
Gastrointestinal conditions
Heart disease
High blood pressure
High cholesterol
Migraines
Osteoporosis
Stroke
None of the above

COLLECT CONTACT INFORMATION FOR HONORARIA

[Use the following definitions for the label links in the choice questions] [For "How long before the cancer grows"]

One of the most important goals of cancer medicines is to keep the cancer from getting worse. We would like you to think about how long the medicine can keep the cancer from growing or getting worse.

[For "Chance of severe skin rash"]

Some medicines for mCRC may cause a skin reaction that will result in a severe rash.

A severe skin rash is an outbreak of at least 20 red solid bumps or blisters on the face, upper back or chest. A severe rash can also be diagnosed when having more than five areas around the body that have skin redness with swelling, each covering about the size of a dime.

With severe rashes, a person will have more than one third of the body with scaly skin that itches, cracks and peels, resulting in serious infections that need to be treated with medicines. A person with a severe rash will also have areas of redness that are painful and cover more than one third of the body.

Itching is constant and affects the person's ability to sleep.

Finally, a person with a severe skin rash will have problems doing some daily activities, like:

- o Bathing
- Dressing and undressing
- o Eating

The rash typically begins within the first 2 weeks of taking a medicine and lasts for up to a month.

[For "Chance of serious bleeding"]

Some medicines for mCRC can cause serious bleeding events. In a serious bleeding event, a person has a large amount of bleeding or bleeds in a critical area of their body such as the

head, spine, near the heart, in the abdomen, or in the joints. People may feel weak and tired and feel a lot of pain.

Most people who experience serious bleeding events will need to be admitted to the hospital and have a blood transfusion or surgery.

[For "Chance of GI perforations"]

Some mCRC medicines may cause gastrointestinal (GI) perforations. GI perforations are holes that develop anywhere in the GI tract, which includes your stomach, intestines, and colon.

GI perforations are more common in patients who have had problems with their GI tract in the past, such as:

- Inflammation of pouches (diverticulitis) or ulcers in the intestine wall
- A recent sigmoidoscopy or colonoscopy (a test that inserts a flexible tube through the rectum to check the large and small intestine)
- Having part of a tumor in the GI tract removed
- Exposure to radiation to treat a tumor in the past
- Blockage of the intestine
- Multiple previous surgeries in the GI tract

With GI perforations you can feel stomach pain, chills, fever, nausea, and vomiting. GI perforations need to be treated immediately. Treatment usually involves surgery to repair the hole. The majority of patients recover completely after surgery.

[For "Chance of a severe heart attack"]

Some medicines for mCRC may cause a severe heart attack. A severe heart attack occurs when the heart stops beating normally and blood does not flow like it should. Without blood flow, the body does not get the oxygen it needs. During a severe heart attack people may lose their breath and pass out. Without medical help, a person having a severe heart attack could die within a few minutes.

Even if a person survives a severe heart attack, their heart will be weaker after the heart attack. With a weaker heart, a person will get tired more quickly and have shortness of breath when doing normal daily activities.

Supplement: Physician Survey

Metastatic Colorectal Cancer Treatment Preferences

Thank you for your interest in this health survey. In this survey we will ask for your professional opinion regarding treatments for patients with metastatic colorectal cancer (mCRC).

If you have any problems or concerns about this survey, please contact AllPoints at 1-800-535-3528 (a toll-free number) or email survey.support@AllPoints.biz and someone will direct your questions to the appropriate researchers at the Research Triangle Institute.

Please answer the following questions to confirm that you are eligible to participate in this survey.

S1.	What is your	primary	medical	specialty?
-----	--------------	---------	---------	------------

Oncology	[ELIGIBLE]
Other	[INELIGIBLE, END SURVEY]

- S2. Have you treated people with metastatic colorectal cancer?
 - YES [CONTINUE]
 - NO [INELIGIBLE, END SURVEY]

Study Purpose

You are one of about 150 people who are being asked to take this survey to help us understand physician preferences for mCRC treatments.

Study Duration

The survey will take about 25 minutes to complete.

Study Details

Research Triangle Institute (RTI) is doing this study for a pharmaceutical company. RTI is a nonprofit research organization in Research Triangle Park, North Carolina.

Possible Risks or Discomforts

If any questions make you uncomfortable, you do not need to answer them.

RTI will protect your responses under its Privacy Policy. RTI will also make every effort to protect your responses. There is a potential risk of disclosure of the survey data, but the data could not be directly tied to you.

Benefits

There are no direct benefits to you for participating in this study. Benefits of this survey apply to the broader population such that it will generate a better understanding of their preferences and potentially lead to a wider choice of treatments.

Confidentiality

Many steps have been taken to protect your information. RTI will report only your responses to the survey, not your name or other contact information. If the results of this study are presented at scientific meetings or published in scientific journals, no information will be included that could identify you or your responses personally.

The Institutional Review Board (IRB) at RTI has reviewed this research. An IRB is a group of people who make sure that the rights of participants in research are protected. The IRB may check records of your activity in this research to see if proper procedures were followed.

Your Rights

Your decision to take part in this research study is completely voluntary. You can refuse to answer any question and still receive an incentive after leaving the interview.

If you have any questions about your rights as a participant of this study, please send an email to the RTI Office of Research Protection at orpe@rti.org.

Background Questions

B1. What is your gender?

- Male
- Female
- B2. In what year were you born?

[Add year dropdown box]

B3. In which state or states are you licensed to practice?

[Add list of states]

- B4. How many years have you been in practice since completing your medical training?
 - Less than 1 year
 - 1—3 years
 - 4—6 years
 - 7—9 years
 - _____10—15 years
 - 16—20 years
 - 21—25 years
 - More than 25 years

B5.	Which of the following describes your practice?	(Check all that apply)
-----	---	------------------------

Office-based private practic	e
------------------------------	---

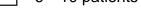
ate practice
ć



- Other
- B6. Approximately how many patients with metastatic colorectal cancer do you treat monthly?



6—10 patients



11—20 patients

21—30	patients
-------	----------

More than 30 patients

B7. Which of the following targeted treatments have you used to treat patients with mCRC? (*Check all that apply*)

Bevacizumab
Cetuximab
Panitumumab
Ziv-aflibercept
Regorafenib
Other targeted agent
None

Features of Treatments for Metastatic Colorectal Cancer

In this survey, we will ask you to evaluate different hypothetical medications to be used in addition to chemotherapy for metastatic colorectal cancer (mCRC) patients. We will ask you to consider the following outcomes of these medications:

- Progression-free survival
- Chance of severe papulopustular rash
- Chance of serious hemorrhage
- Chance of cardiopulmonary arrest
- Chance of gastrointestinal (GI) perforations

We will provide some additional information on these outcomes in the next few pages.

Treatment Feature: Chance of Severe Papulopustular Rash

Some medications for colorectal cancer may cause a severe papulopustular rash. Symptoms of a severe papulopustular rash typically appear within the first 2 weeks of taking the medication and last for up to a month.

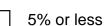
A patient with a severe papulopustular rash will have more than 20 papules or pustules; or more than 5 areas of erythema/edema that are less than 1cm in size. These papules or pustules may include pain and pruritus.

With a severe papulopustular rash, the patient will experience painful erythema covering more than 30% of the body. They will also experience severe, widespread, and constant pruritus interfering with sleep. Scaling and flaking on the skin will cover more than 30% of the body causing fissuring and cracking that lead to signs of super infection.

A patient with a severe papulopustular rash will experience limitations in activities of daily life, such as bathing, dressing and undressing, and feeding him or herself.

1. What percentage of your mCRC patients reported having severe skin rashes during treatment?





- More than 5% but less than 10%
 - More than 10% but less than 25%
- More than 25%
- Other
- 2. Do you recommend prophylactic treatment for skin rashes to patients with mCRC?
 -] Yes
 -] No

Risk of Side Effects

In this survey we will use some graphics to help you evaluate the risk of side effects.

Every figure in the pictures below represents 1 person who is taking a mCRC medication.



There are 100 figures in the picture. The figures shown in color indicate people who will get a side effect while taking a mCRC medication. The figures shown in gray indicate the number of people who will not get a side effect while taking a mCRC medication.

The graphs below indicate the risk of experiencing an adverse event with two different medications to treat mCRC patients (Medication A and Medication B).

Medication feature	Medication A	Medication B
Risk of an adverse event	20 cases out of 100 (20%)	10 cases out of 100 (10%)

3. How many cases of adverse events would you expect to see if 100 patients take Medication A?

40 cases	out of	100	(40%)
----------	--------	-----	-------

20 cases out of 100 (20%)

10 cases out of 100 (10%	5)
--------------------------	----

5 cases out of 100	(5%)
--------------------	------

0 cases out of 100 (0%)

[Show this page if Q3 is not 20%]

Medication feature	Medication A	Medication B
Risk of an adverse event	20 cases out of 100 (20%)	10 cases out of 100 (10%)

You said that [response to Q3] people would have a side effect. Given your response, we would like to remind you that the figures shown in color represent people who will have a side effect.

Each figure in the boxes above represents one person who has being diagnosed with mCRC and is currently treated. There are 100 figures in the box. For Medication A, the figures shown in color indicate that 20 people would experience an adverse event after taking Medication A. Therefore, the correct answer is 20 out of 100 (20%).

Treatment Feature: Chance of Serious Hemorrhage

Some medications for colorectal cancer may cause serious hemorrhages. Serious hemorrhages include:

- Bleeding in large quantities (causing a drop in hemoglobin of at least 2 g/dl and/or leading to a transfusion of 2 or more units of packed red blood cells or whole blood), or
- Bleeding in a critical site (subdural, subarachnoid, epidural, intraspinal, intraocular, pericardial, intra-articular, intramuscular with compartment syndrome, or retroperitoneal).
- 4. Which of the following bleeding events is most concerning to you?
 - Subdural bleeding
 - Subarachnoid bleeding
 - Epidural bleeding
 - Intraspinal bleeding
 - Intraocular bleeding



- Intra-articular bleeding
- Intramuscular bleeding with compartment syndrome
- Retroperitoneal bleeding

Patient Profile

In the following questions, we will ask you to evaluate mCRC medications for the following patient. The patient:

- is male
- is 65 years of age
- has hypertension which is well controlled
- takes atorvastatin for hypercholesterolemia
- is active and has no major health concerns

Medication Choices

We will show you [#] choice questions.

The medications you are asked to consider in this section may be different than medications that are currently available.

Even if neither mCRC medication is optimal, please indicate which of the two medications shown would be the better choice for the patient, in your professional opinion.

In selecting the better medication, please do not consider formulary status or costs of the medications to your practice or institution or to your patients.

Choice question [#]

[Add this text before the first choice question]

In the following questions, we will ask you to evaluate mCRC medications for a patient who is male, 65 years of age and has hypertension that is well controlled. The patient takes atorvastatin for hypercholesterolemia and is active and has no major health concerns.

[Add this text before the second and third choice questions]

Remember, the patient is male, 65 years of age and has hypertension that is well controlled. The patient takes atorvastatin for hypercholesterolemia and is active and has no major health concerns.

Medication Feature	Medication A	Medication B
Progression-free survival	6 months	8 months
Chance of severe papulopustular rash		
Chance of serious hemorrhage	20% (20 out of 100)	20% (20 out of 100)
Chance of GI perforations	1% (1 out of 100)	
Chance of cardiopulmonary arrest	2% (2 out of 100)	1% (1 out of 100)

Which medication would you prescribe to this patient if these were the only treatments available?	

Note – Example medication profiles. The actual medication profiles will be created following and experimental design. THESE QUESTIONS WILL BE USED TO ESTIMATE PREFERENCE WEIGHTS.

Suppose you were presented with the following options today.

5. Would you rather live 10 years with severe rash or 7 years in perfect health?



- 10 years with severe rash
- \square
 - 7 years in perfect health [Skip to question 7]
- 6. Would you rather live 8 years with severe rash or 7 years in perfect health?
 - 8 years with severe rash [Skip to the next page]
 - 7 years in perfect health [Skip to the next page]
- 7. Would you rather live 12 years with severe rash or 7 years in perfect health?



 \square

12 years with severe rash



Q8, 9, 10 – SHOW RESPONDENT 2% OR 5% OR 9% CONSISTENTLY ACROSS THESE 3 QUESTIONS:

Suppose you were presented with the following options today.

•		d you rather live 10 years with a [randomize across respondents: 2%; 5%; 9%] are of <u>serious hemorrhage</u> or 7 years in perfect health?
		10 years with a [randomize across respondents: 2%; 5%; 9%] chance of serious hemorrhage
		7 years in perfect health [Skip to question 10]
•		d you rather live 8 years with a [randomize across respondents: 2%; 5%; 9%] are of <u>serious hemorrhage</u> events or 7 years in perfect health?
		8 years with a [randomize across respondents: 2%; 5%; 9%] chance of serious hemorrhage [Skip to the next page]
		7 years in perfect health [Skip to the next page]

10. Would you rather live 12 years with a [randomize across respondents: 2%; 5%; 9%] chance of serious hemorrhage or 7 years in perfect health?



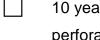
12 years with a [randomize across respondents: 2%; 5%; 9%] chance of serious hemorrhage



Q11, 12, 13 – SHOW RESPONDENT 2% OR 5% OR 9% CONSISTENTLY ACROSS **THESE 3 QUESTIONS:**

Suppose you were presented with the following options today.

11. Would you rather live 10 years with a [randomize across respondents: 2%; 5%; 9%] chance of GI perforations or 7 years in perfect health?



10 years with a [randomize across respondents: 2%; 5%; 9%] chance of GI perforations



7 years in perfect health [Skip to question 13]

12. Would you rather live 8 years with a [randomize across respondents: 2%; 5%; 9%] chance of GI perforations or 7 years in perfect health?



8 years with a [randomize across respondents: 2%; 5%; 9%] chance of GI perforations [Skip to the next page]



7 years in perfect health [Skip to the next page]

13. Would you rather live 12 years with a [randomize across respondents: 2%; 5%; 9%] chance of GI perforations or 7 years in perfect health?



12 years with a [randomize across respondents: 2%; 5%; 9%] chance of GI perforations



Q14, 15, 16 – SHOW RESPONDENT 2% OR 5% OR 9% CONSISTENTLY ACROSS THESE 3 QUESTIONS:

Suppose you were presented with the following options today.

14. Would you rather live 10 years with a [randomize across respondents: 2%; 5%; 9%] chance of <u>cardiopulmonary arrest</u> or 7 years in perfect health?

10 years with a [randomize across respondents: 2%; 5%; 9%] chance of cardiopulmonary arrest



- 7 years in perfect health [Skip to question 16]
- 15. Would you rather live 8 years with a [randomize across respondents: 2%; 5%; 9%] chance of <u>cardiopulmonary arrest</u> or 7 years in perfect health?

8 years with a [randomize across respondents: 2%; 5%; 9%] chance of cardiopulmonary arrest [Skip to the next page]



- 7 years in perfect health [Skip to the next page]
- 16. Would you rather live 12 years with a [randomize across respondents: 2%; 5%; 9%] chance of <u>cardiopulmonary arrest</u> or 7 years in perfect health?

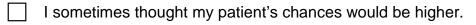


12 years with a [randomize across respondents: 2%; 5%; 9%] chance of cardiopulmonary arrest



Your Experience with the Choice Questions in this Survey

17. When considering the choice questions that showed different chances of side effects, did you think that your patient's chances were different than the chances shown?





I thought my patient's chances would be about the same.



- I did not think about my patient's chances.
- 18. Please rate your agreement with the following statement:

When I saw medications that would increase the chance that my patient would get a severe rash, I thought I could do something to lower my patient's chances, by prescribing additional treatments.



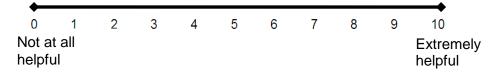
- I strongly agree
- I agree
- I neither agree nor disagree
- I disagree
- I strongly disagree

Patient Education

19. How do you usually inform your patients about the potential side effects of mCRC treatments? (<i>Check all that apply</i>)		
	I discuss potential side effects of treatments during the patient's visit	
	Our office staff shares educational materials about the prescribed treatments	
	I recommend internet sites where the patient can find more information if they	
	choose to	
	Other	
	v satisfied are you with the educational materials available to patients on the ential side effects of treatments?	
	Very satisfied	
	Somewhat satisfied	
	Neither satisfied or dissatisfied	
	Somewhat dissatisfied	
	Very dissatisfied	

21. On the scale from 0 to 10, please circle the number that best describes how helpful it would be to have additional educational materials to talk to your patients about the potential side effects of their mCRC treatment?

INCLUDE NUMBERS AND RADIO BUTTONS



COLLECT CONTACT INFO FOR HONORARIA