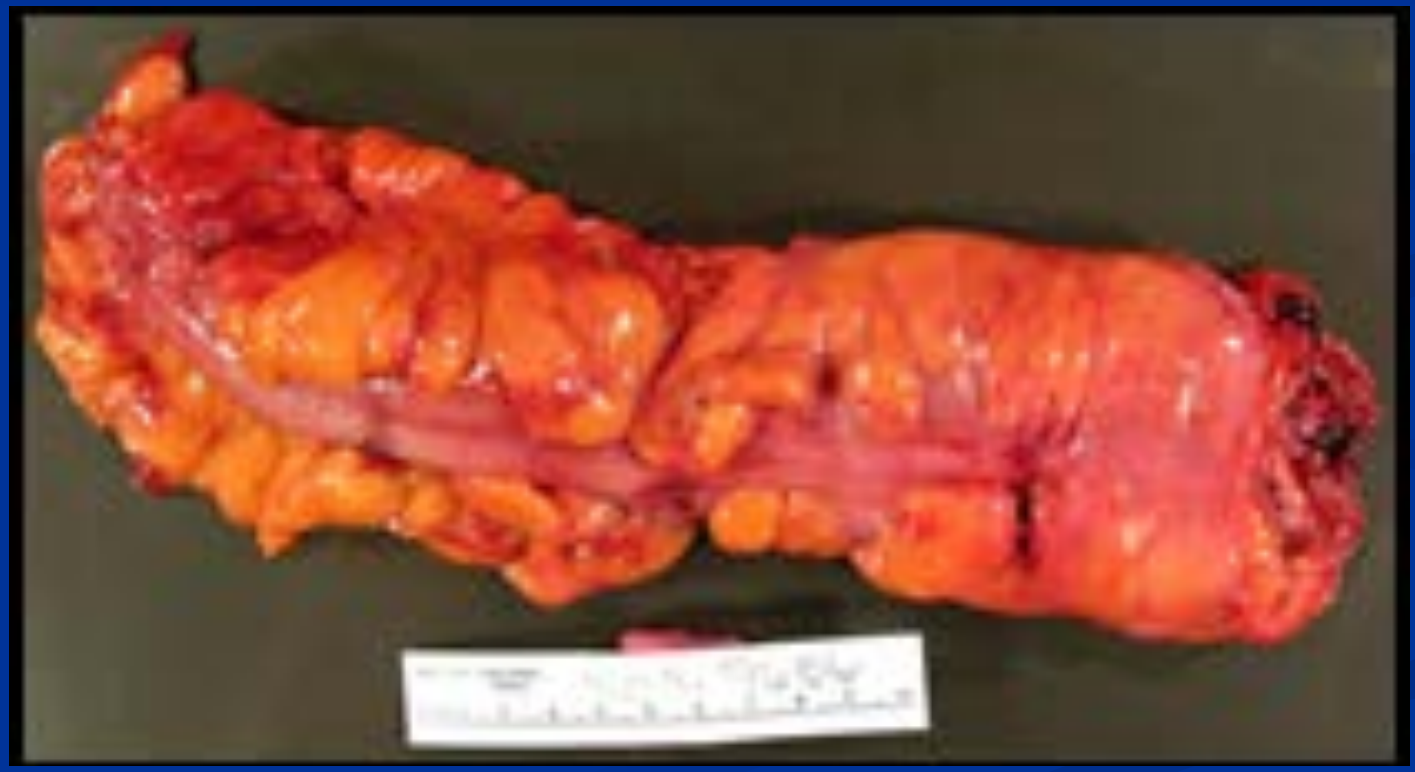
PROSPECT

Preoperative Radiation Or Selective Preoperative radiation and Evaluation before Chemotherapy and TME

N1048 Protocol available on CTSU.org

Rectal Cancer

- 39,870 new cases of rectal cancer in the US in 2011 (ACS estimate)



PROSPECT (N1048)

Standard of Care

- For 20+ years, the standard of care for Stage II (T3/T4N0) and Stage III (TanyN1/N2) rectal cancer:

Chemotherapy

Radiation

Surgery

The Question Is…

- Can radiation be avoided in some patients without compromising (and possibly improving) outcomes?

Chemotherapy

Surgery

Pros and Cons of Pelvic Radiation Therapy

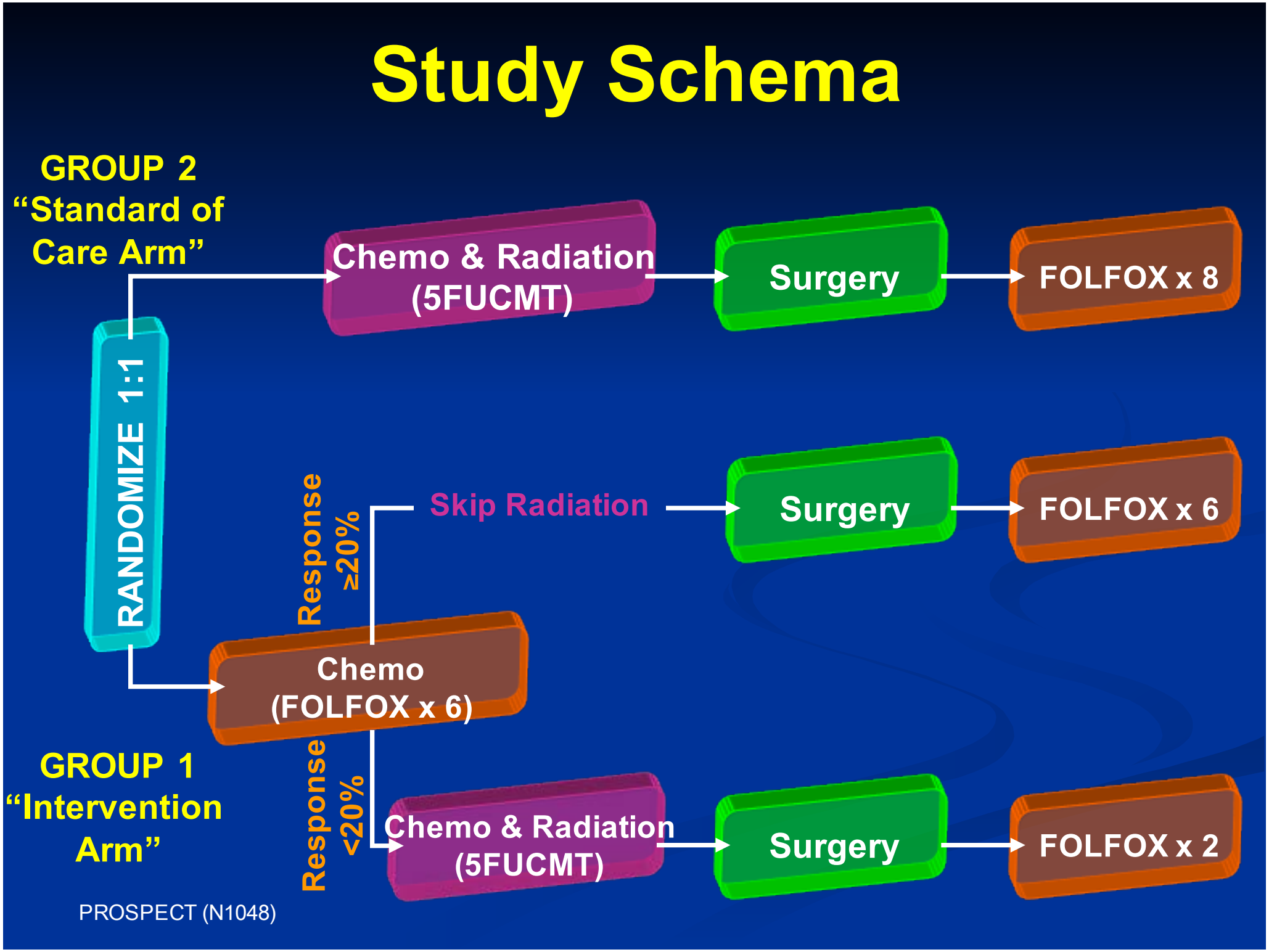
PROS:

- Decrease local recurrence rates
- Increase the potential for rectal sphincter preservation

CONS:

- Inconvenient - requires 28 daily visits
- Loss bowel function
- Bladder and sexual dysfunction
- Loss of fertility
- Diminished bone marrow reserve
- Fibrosis
- Autonomic nerve injury
- Delays systemic chemo

Study Schema



Study Endpoints

Primary Outcomes:

- R0 Resection Rate
- Time to local recurrence
- Disease free survival

Secondary Outcomes:

- Pathologic complete response rate
- Overall survival
- Quality of life
- Clinician and patient reported treatment toxicity
- Rates of receiving 5FUCMT

Eligibility Criteria

Inclusion:

- Age 18+
- Rectal adenocarcinoma
- Baseline Clinical staging (AJCC7*): T2N1, T3N0, T3N1

Exclusion:

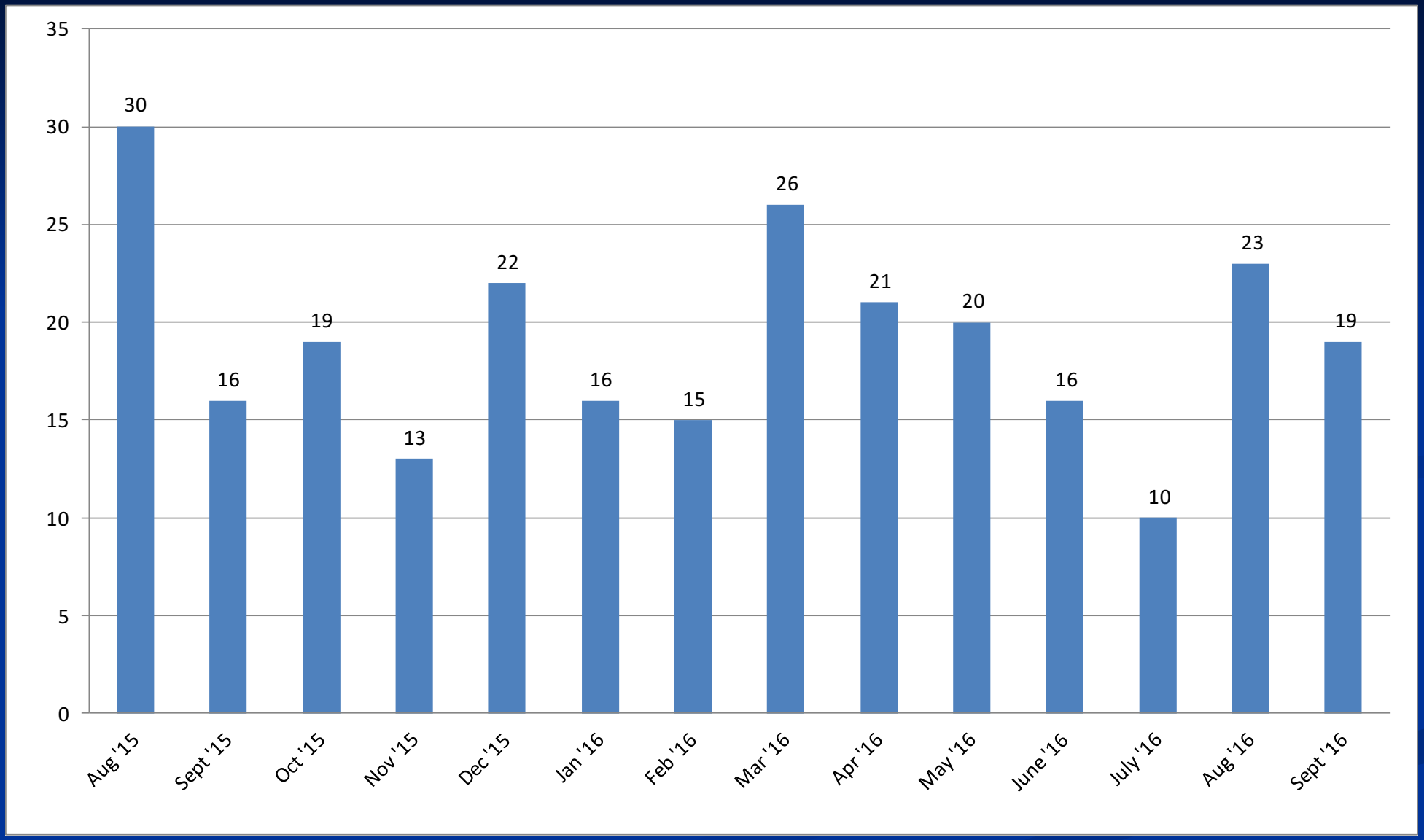
- Clinical T4 tumors
- Tumor is causing bowel obstruction
- Had previous pelvic radiation (ever), chemo or other cancer (in last 5 years)
- Pregnant/Nursing

*http://www.cancerstaging.org/staging/posters/colon8.5x11.pdf
**See protocol for full list of eligibility criteria
T2(3)=Primary tumor invades muscularis propria (into pericolorectal tissues)
T4=Primary tumor penetrates to surface of visceral peritoneu/invates other organs
N0(1)=No (one, two, or three) metastasis in regional lymph nodes

Major CRA Tasks

- Completing and submitting study forms via RAVE
- Shipping blood, tissues, and images
- Training patients how to report their symptoms from home via phone or web

Recent Monthly PROSPECT Accrual



Current Study-Wide Accrual: **653**

Study-Wide Accrual Goal: 1066

Top Accruing Sites – Thank you!

Site	Total Accrual to date
Kaiser Permanente-Various Locations	46
Dana-Farber Cancer Institute	18
MD Anderson	18
Fox Chase	17
CancerCare Manitoba	17
John H Stroger Jr Hospital of Cook County	15
University of Rochester	15
Memorial Sloan Kettering	13
Abington Memorial	11
Ben Taub (Baylor)	11
Roswell Park	10

Please continue to accrue!

- Current Study-Wide Accrual: 653
- Study-Wide Accrual Goal: 1066

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PROSPECT
N1048: Rectal Cancer
Clinical Trial

PROSPECT
N1048: Rectal Cancer Clinical Trial

Contact:

PROSPECT Protocol Coordinator
Morgen Alexander-Young
malexanderyoung@uchicago.edu

Improving Informed Consent for Palliative Chemotherapy

Project leaders:
Deb Schrag, PI
Andrea Enzinger, PI
Liz Frank, Patient Advocate
Laura Porter, Patient Advocate

Background

- Although patients typically sign an informed consent (IC) document prior to starting treatment (even if not on a clinical trial), many lack the minimal understanding required for an informed decision.

- 81% of patients in a large national survey with metastatic colorectal cancer falsely believed that palliative chemotherapy could cure their cancer (NEJM, 2012).

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Informed Consent

- Consent forms are:
  - legalistic disclosures of all possible risks
  - without any meaningful information about benefits
  - devoid of the patient perspective

- Chemo education materials:
  - focus on individual drugs rather than regimens
  - describe the toxicities of individual drugs rather than regimens

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Overall Study Purpose

- Develop IC tools for common palliative chemotherapy regimens used to treat colorectal cancer that improve upon available resources in 4 critical respects:
    1. organized by regimen rather than individual drugs
    2. use video and written formats
    3. balance information on risks and benefits
    4. include patient voices

- The “informed consent” moment represents a strategic opportunity to empower patients with knowledge about the risks and benefits of their treatment options.

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RESEARCH in PROGRESS

- The work presented today is research in progress.
- Will describe development of an intervention and share the intervention.
- The intervention is currently being tested, we launched an RCT in June 2015.
- Because this is in process and is being evaluated in the context of an RCT, please DO NOT SHARE the intervention.

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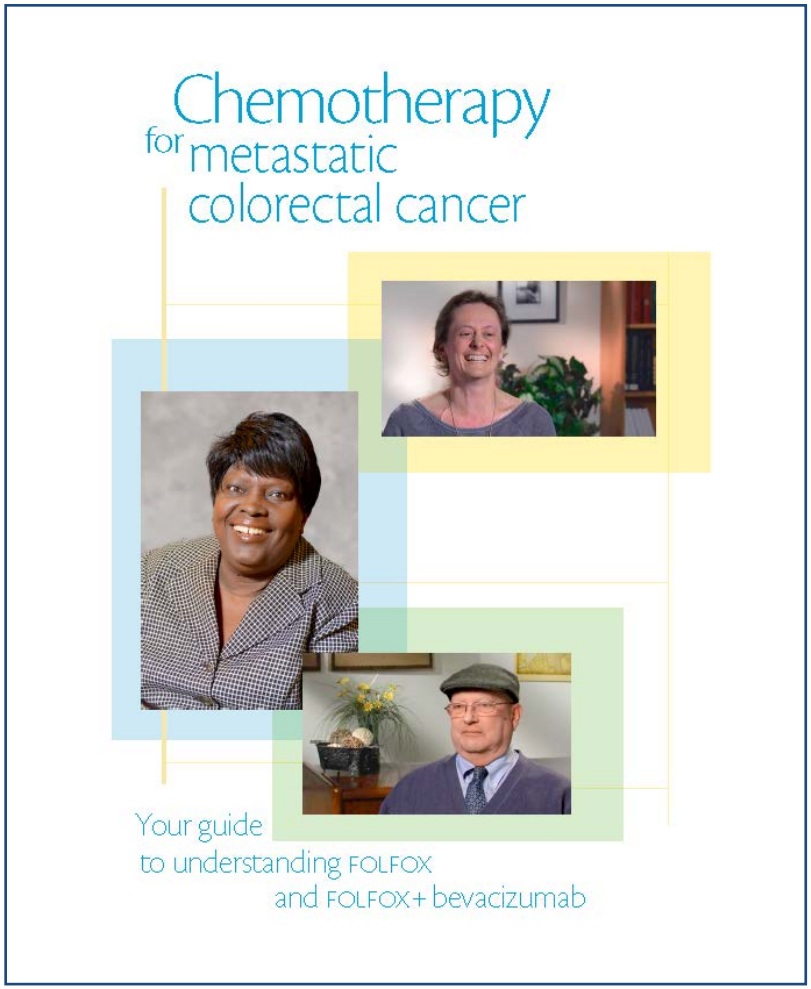
Part 1: Develop IC Tools Booklet & Video



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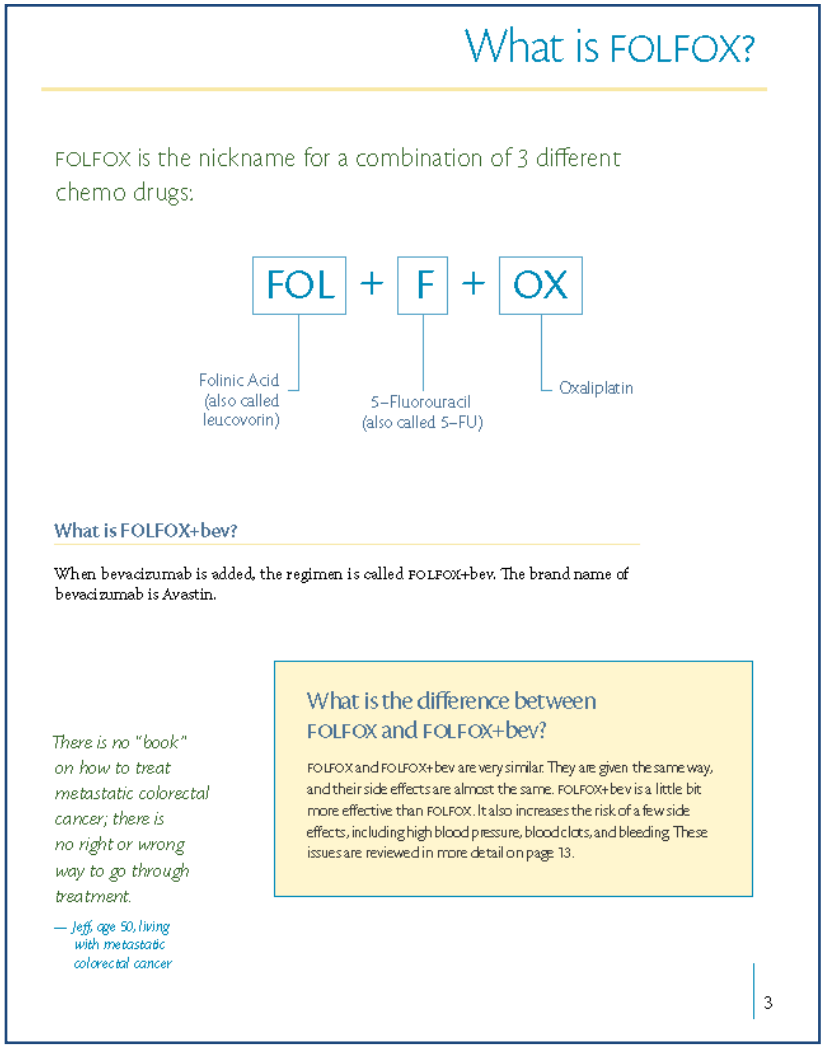
Booklet Excerpts



What is FOLFOX?

FOLFOX is the nickname for a combination of 3 different chemo drugs:

FOL + F + OX

- FOL: Folinic Acid (also called leucovorin)
- F: 5-Fluorouracil (also called 5-FU)
- OX: Oxaliplatin

What is FOLFOX+bev?

When bevacizumab is added, the regimen is called FOLFOX+bev. The brand name of bevacizumab is Avastin.

There is no "book" on how to treat metastatic colorectal cancer; there is no right or wrong way to go through treatment.

— Jeff, age 50, living with metastatic colorectal cancer

What is the difference between FOLFOX and FOLFOX+bev?

FOLFOX and FOLFOX+bev are very similar. They are given the same way, and their side effects are almost the same. FOLFOX+bev is a little bit more effective than FOLFOX. It also increases the risk of a few side effects, including high blood pressure, blood clots, and bleeding. These issues are reviewed in more detail on page 13.

3

Organized by regimen rather than individual drugs

Includes patient voices; Quotes from actual people living with mCRC

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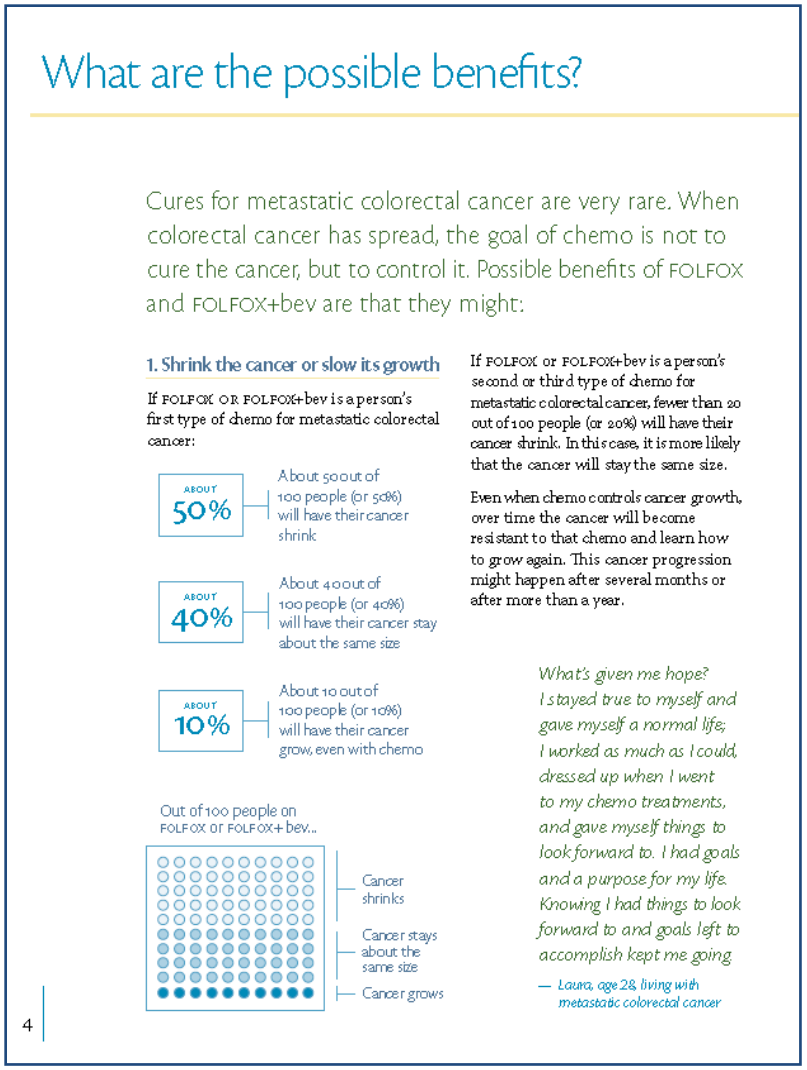
Booklet Excerpts



What are the possible benefits?

Cures for metastatic colorectal cancer are very rare. When colorectal cancer has spread, the goal of chemo is not to cure the cancer, but to control it. Possible benefits of FOLFOX and FOLFOX+bev are that they might:

1. Shrink the cancer or slow its growth

If FOLFOX OR FOLFOX+bev is a person's first type of chemo for metastatic colorectal cancer:

ABOUT 50% — About 50 out of 100 people (or 50%) will have their cancer shrink

ABOUT 40% — About 40 out of 100 people (or 40%) will have their cancer stay about the same size

ABOUT 10% — About 10 out of 100 people (or 10%) will have their cancer grow, even with chemo

If FOLFOX or FOLFOX+bev is a person's second or third type of chemo for metastatic colorectal cancer, fewer than 20 out of 100 people (or 20%) will have their cancer shrink. In this case, it is more likely that the cancer will stay the same size.

Even when chemo controls cancer growth, over time the cancer will become resistant to that chemo and learn how to grow again. This cancer progression might happen after several months or after more than a year.

Out of 100 people on FOLFOX or FOLFOX+bev...

What's given me hope? I stayed true to myself and gave myself a normal life; I worked as much as I could, dressed up when I went to my chemo treatments, and gave myself things to look forward to. I had goals and a purpose for my life. Knowing I had things to look forward to and goals left to accomplish kept me going.

— *Laura, age 28, living with metastatic colorectal cancer*

4

Balances information on risks and benefits

Uses graphics in addition to text

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Booklet Excerpts

How will I be given FOLFOX or FOLFOX+bev?

FOLFOX (and FOLFOX+bev) is an intravenous (I.V.) chemo, given through a vein. It is given every 2 weeks. This is called a 2-week "cycle." The treatment itself lasts for 2 days.

Where will I receive FOLFOX or FOLFOX+bev?

At your cancer clinic. You will get the first part of FOLFOX or FOLFOX+bev in the infusion area of your clinic. This takes 2–3 hours.

AND

At your home. Before you leave the clinic, your nurse will set up a small chemo pump that you will wear home. The chemo pump will infuse one chemo drug (5-FU) over the next 2 days. While the pump is infusing, you can do most of the things you usually do, like light housework, deskwork, walking, driving, or shopping. For these 2 days, you should not shower or let the pump get wet.

How many cycles of FOLFOX or FOLFOX+bev will I get?

There is no set number of cycles. Most people continue to get chemo as long as it's working and as long as the side effects aren't bothering them too much.

What is a port?

To get FOLFOX or FOLFOX+bev, you will need to have a port. A port is an I.V. that is completely hidden under the skin on your chest. A port gives your nurse easier and safer access to your veins for blood work, medication, and chemo. To use the port, a nurse will push a thin needle through your skin into the port. When the infusion is finished, the needle is removed. For more information, please see page 18.

Paul, age 75, living with metastatic colorectal cancer

Start with logistics

What happens during a typical 2-week cycle?

DAY 1

Plan to spend about half a day at your clinic. On this day you will:

- Have your blood drawn
- See your oncology provider
- Spend 2–3 hours in the infusion area, where your nurse will:
  - Give you anti-nausea medicines
  - Give you chemo
  - Set up your home chemo pump

DAY 2

The pump will continue to infuse 5-FU chemo at home.

DAY 3

The pump will finish infusing the 5-FU after a total of 46 hours. Your nurse will shut off your pump and remove the needle from your port. Many people learn to do this at home.

DAY 4–14

You are finished with chemo until your next cycle.

Booklet Excerpts

How will I feel?

When some people hear the word "chemo," they think of being very sick. That is *not* typical for FOLFOX or FOLFOX+ bev. Side effects can usually be treated with medicine. The goal is for you to feel well for most of your cycle.

During the first 4 or 5 days of your cycle, you will probably feel tired and have a poor appetite and mild nausea. Oxaliplatin will make your hands, feet, and throat very sensitive to cold. It will also cause numbness and tingling in your fingers and toes (called neuropathy). You will

probably start feeling better
or 5th day, and most people f
normal by the 2nd week of th
Some of these symptoms get
being on chemo for many mo
this happens, your doctor mi
the chemo to help you feel be

What are the possible side effects?

FOLFOX (or FOLFOX+bev) has many possible side effects. Every person reacts to chemo differently. Just because a side effect is listed does not mean that you will have it. Sometimes side effects are

mild, and sometimes they ar
very rare cases, side effects c
enough to cause death. Most
are temporary and will go av
you stop chemo.

ALWAYS TELL your doctor or nu
about your side effects so that
they can help you manage the

8

Balances information on risks and benefits

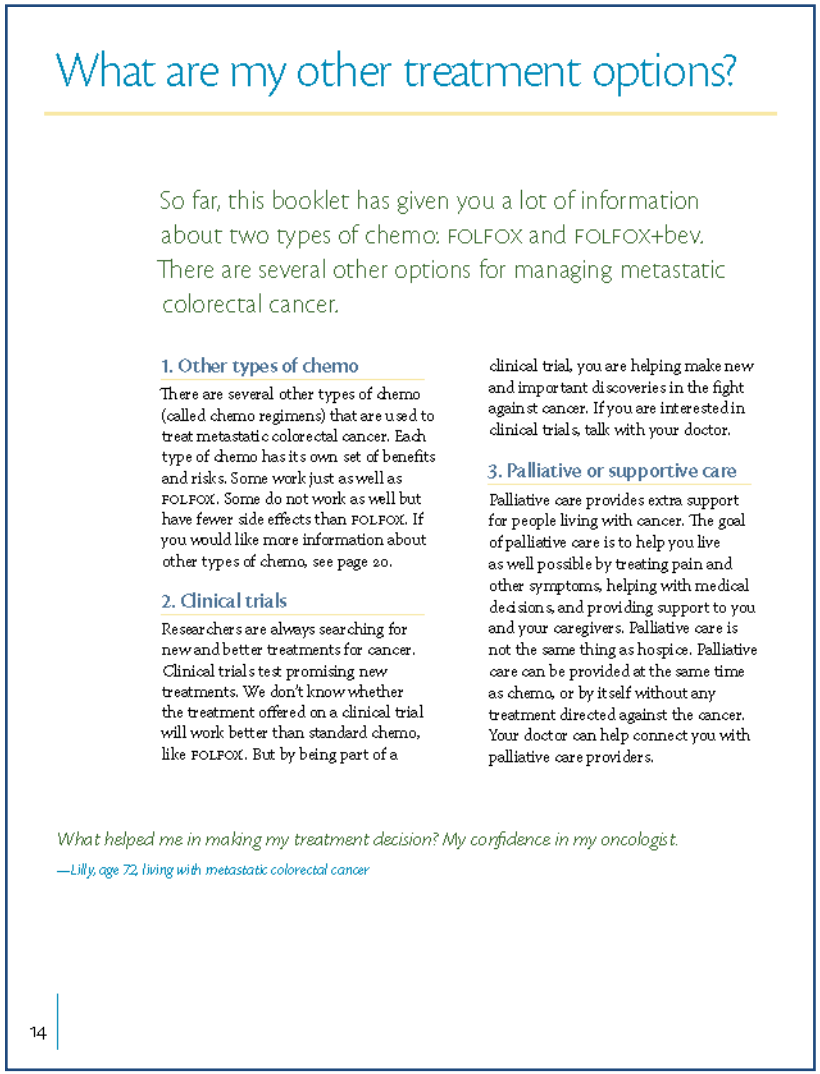
Includes "What you can do about side effects"

Common side effects

If 100 people get FOLFOX or FOLFOX+bev, between 50 and 100 people (or 50-100% of them) may have these side effects

SIDE EFFECT	WHAT YOU CAN DO ABOUT IT
Nausea or vomiting Most people have mild nausea and may sometimes vomit. Very few people have severe nausea or vomiting.	Your doctor will prescribe anti-nausea medicine Drink plenty of fluids (8–12 glasses per day) Eat small, frequent meals Eat bland foods
Diarrhea About half of people will have occasional loose or watery stools. Severe diarrhea is uncommon.	Drink plenty of fluids (8–12 glasses per day) Avoid high-fiber foods Use anti-diarrhea medicine like Loperamide (Imodium)
Fatigue, tiredness, or lack of energy	Sleep at least 8 hours at night Rest or take short naps Take short walks or do light exercise
Sensitivity to cold	Drink beverages at room temperature for 3–5 days Use gloves when you reach into the freezer or fridge If it is cold outside, dress warmly and wear gloves and thick socks
Neuropathy (numbness or tingling in your fingers and toes)	Tell your doctor about these symptoms at every visit Your doctor may adjust your chemo to prevent permanent symptoms

Booklet Excerpts



What are my other treatment options?

So far, this booklet has given you a lot of information about two types of chemo: FOLFOX and FOLFOX+bev. There are several other options for managing metastatic colorectal cancer.

1. Other types of chemo

There are several other types of chemo (called chemo regimens) that are used to treat metastatic colorectal cancer. Each type of chemo has its own set of benefits and risks. Some work just as well as FOLFOX. Some do not work as well but have fewer side effects than FOLFOX. If you would like more information about other types of chemo, see page 20.

2. Clinical trials

Researchers are always searching for new and better treatments for cancer. Clinical trials test promising new treatments. We don't know whether the treatment offered on a clinical trial will work better than standard chemo, like FOLFOX. But by being part of a clinical trial, you are helping make new and important discoveries in the fight against cancer. If you are interested in clinical trials, talk with your doctor.

3. Palliative or supportive care

Palliative care provides extra support for people living with cancer. The goal of palliative care is to help you live as well possible by treating pain and other symptoms, helping with medical decisions, and providing support to you and your caregivers. Palliative care is not the same thing as hospice. Palliative care can be provided at the same time as chemo, or by itself without any treatment directed against the cancer. Your doctor can help connect you with palliative care providers.

What helped me in making my treatment decision? My confidence in my oncologist.

—Lilly, age 72, living with metastatic colorectal cancer

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Presents alternative options to empower patients to make informed decisions about their care

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Booklet Excerpts

How might FOLFOX or FOLFOX+bev affect the length of my life?

On average, people with metastatic colorectal cancer who receive FOLFOX or FOLFOX+bev live for about 2 to 2½ years after their diagnosis. This means that half of people will live longer than this, and half will live for less time. People who don't get any treatment live for an average of about 6 to 9 months.

More information about how long people with metastatic colorectal cancer typically live:

If 100 people with metastatic colorectal cancer are treated with FOLFOX or FOLFOX+bev:

1 YEAR AFTER DIAGNOSIS — about **75 people out of 100** (or 75% of them) will still be living

2 YEARS AFTER DIAGNOSIS — about **50 people out of 100** (or 50% of them) will still be living

5 YEARS AFTER DIAGNOSIS — about **10 people out of 100** (or 10% of them) will still be living

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- **Provides information on life expectancy**
- **Encourages patients to ask for more information**

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Booklet Excerpts

Frequently Asked Questions

How will I know if FOLFOX or FOLFOX+bev is working? You will probably have a CT scan or MRI every 2 to 3 months to make sure that the treatment is working.

How long will I continue on FOLFOX or FOLFOX+bev? How long your treatment lasts will depend on how well it works and how well you feel on it. If a scan shows any cancer growth, your doctor will talk to you about making a change in your chemo. If your side effects are too much, changing your treatment may also make sense.

Can I take a break from chemo? Yes. Most people will delay or skip a few treatments to enjoy holidays, vacations, or just to get away. If you need a longer break, your doctor will talk to you about the pros and cons of taking more time off.

How is a port placed? A doctor will place the port during a very brief surgical procedure. You will be given medication during the procedure to help you feel comfortable, similar to what you may have had during a colonoscopy.

How do I take care of my port? While the port is in use, do not let it get wet. (It is best not to take showers or baths during the 2 days your port is in use.) Avoid strenuous activities that might accidentally disconnect the needle from the port. If your needle does come out accidentally, call your doctor or nurse immediately. When the port is not in use, there are no limitations to your usual activities, including bathing, swimming, or sports. If there is a time when you are not regularly using your port, a nurse will need to flush it with fluid every 4–6 weeks to keep it working well.

Is it painful to "access" the port? "Accessing" the port means putting a needle into it. Most people report a mild pinch, like a bee sting, from the needle prick. If you find accessing the port very painful, a numbing cream can be used.

Do I need to take special precautions to prevent infections? No, you can go into public without any special precautions. You don't need to wear a mask or gloves in public. It is also fine to spend time with small children. Stay away from people who have the flu or a bad cold.

Can I work while I'm on chemo? Yes, many people continue to work while on chemo. If you choose to work, you will probably need some flexibility in your work schedule. It can be hard to work during the first few days of each chemo cycle because of the pump and because of side effects. Some people choose to stop working because of the symptoms of their cancer, the time commitment of the treatment, or changes in their personal priorities. If you are thinking about taking temporary or permanent leave from your job, talk to your doctor,

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FAQs were contributed by actual patients living with metastatic colorectal cancer

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Video Screenshot – The doctor's voice

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Video Screenshot – The nurse's voice

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Video Screenshot – The patient's voice

Currently, 5 Tools Exist

1. Gemcitabine

   Advanced Pancreatic Cancer(booklet & video)

2. FOLFIRINOX

   Advanced Pancreatic Cancer (booklet & video)

3. Gemcitabine + nab-paclitaxel

   Advanced Pancreatic Cancer (booklet & video)

4. FOLFOX +/- bevacizumab

   Metastatic Colorectal Cancer (booklet & video)

5. FOLFIRI +/- bevacizumab

   Metastatic Colorectal Cancer (booklet & video)

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Part 2: Acceptability Testing and Patient Stakeholder-Driven Refinement IC Tools

1. **Two patient stakeholder panels (one local and one national)** have provided feedback and suggestions at each step of development.

2. We presented the informed consent tools to **patient advocate attendees at the ASCO** Annual Meeting (Saturday, May 31, 2014) and requested feedback through audience response (i.e., handheld remote control clickers) and discussion.

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Patients engaged in this project


ASCO
50TH ANNUAL MEETING
SCIENCE & SOCIETY
Information
ASCO
Patient Advocate Lounge

Video

	Number of respondents	Percent who responded "agree" or "strongly agree"
The video is well organized and easy to follow.	54	85%
Information about how FOLFOX+/-bev chemotherapy is given is presented clearly.	57	95%
Information about the risks of chemotherapy and benefits of chemotherapy are well balanced.	57	75%
The discussion of treatment alternatives is unbiased.	56	52%
Hearing from actual patients strengthens the video.	57	100%

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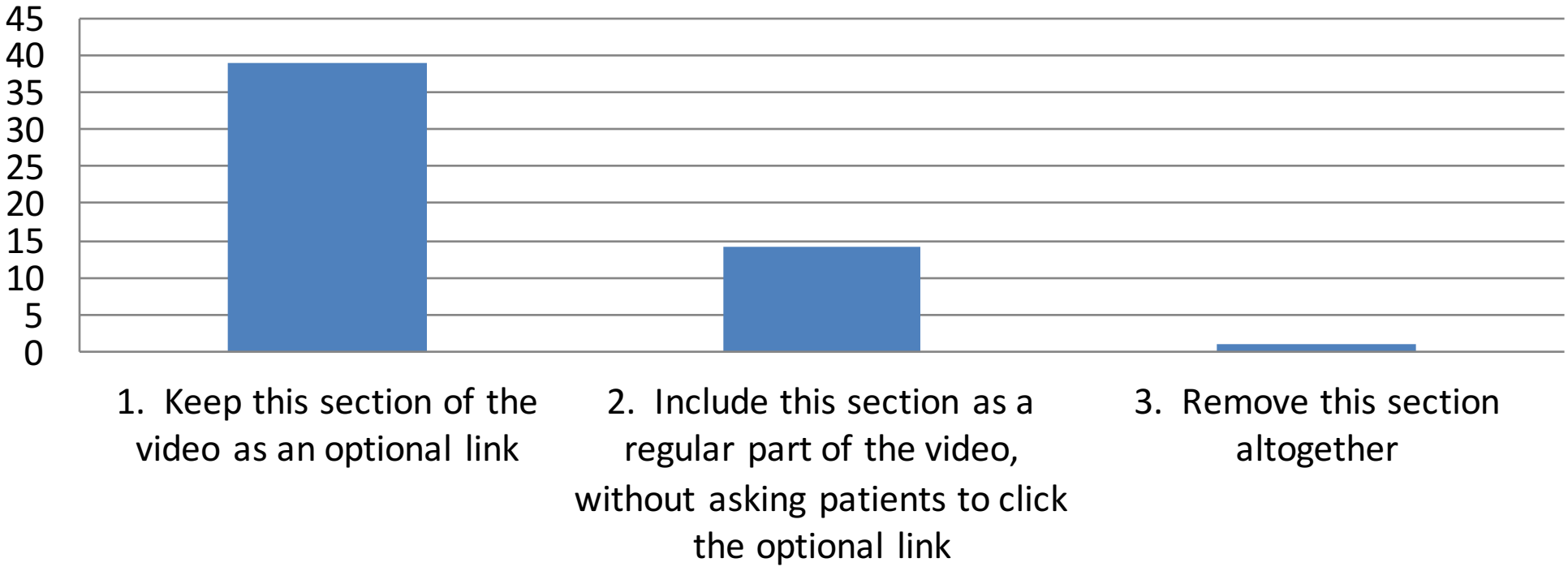
Video

In your opinion – how should we include information about likelihood of benefits (including life expectancy) within the video?



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Booklet

	Number of respondents	Percent who responded "agree" or "strongly agree"
The booklet is well organized and easy to follow.	40	68%
Information about how FOLFOX+/-bev chemotherapy is given is presented clearly.	42	90%
Information about the risks of chemotherapy and benefits of chemotherapy are well balanced.	40	65%
The discussion of treatment alternatives is unbiased.	37	43%

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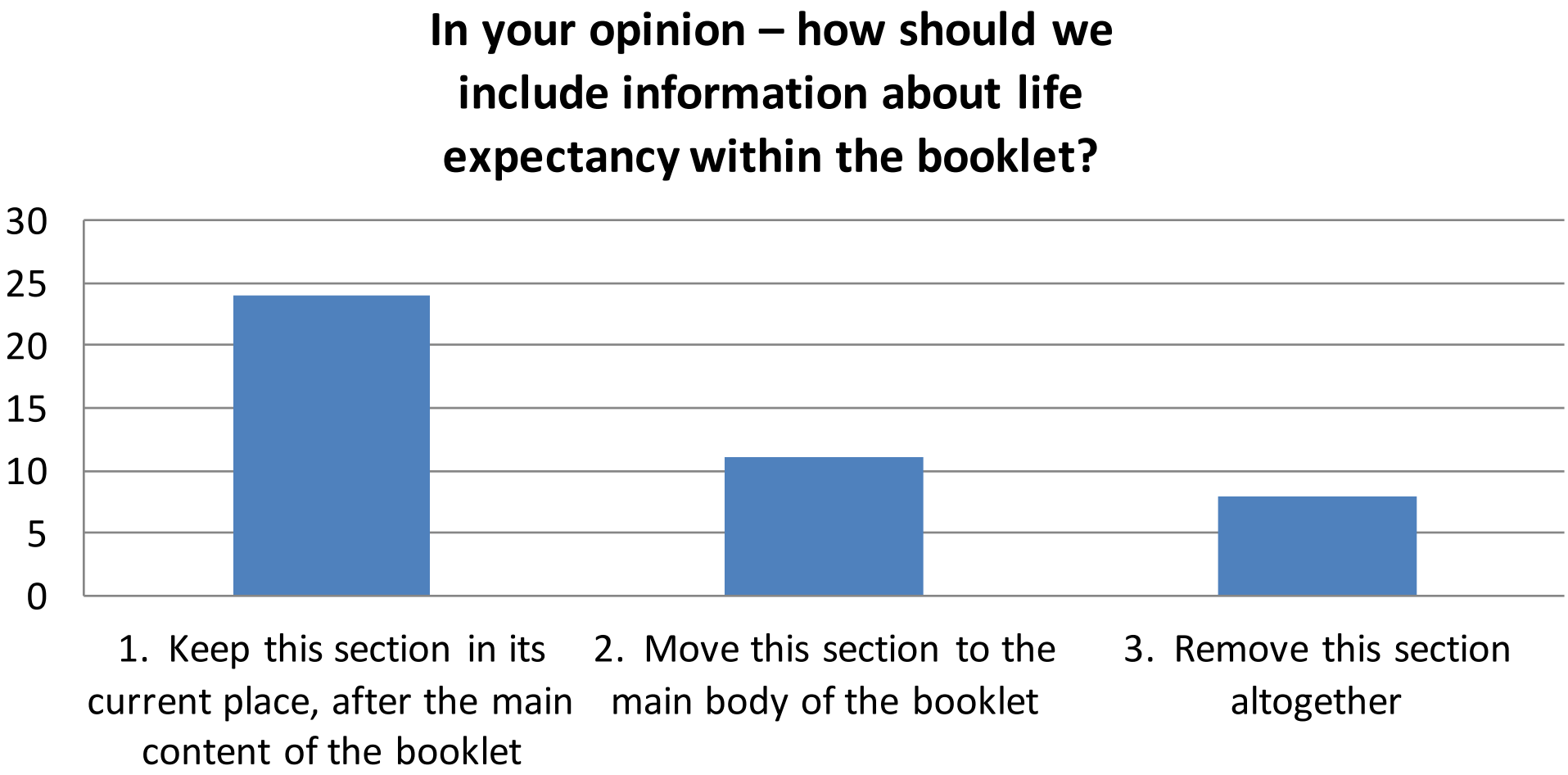
Booklet


In your opinion – how should we include information about life expectancy within the booklet?
30
25
20
15
10
5
0
1. Keep this section in its current place, after the main content of the booklet
2. Move this section to the main body of the booklet
3. Remove this section altogether

Life Expectancy and Response Rates

	Number of respondents	Percent who responded "agree" or "strongly agree"
Information about life expectancy is important to most patients with advanced cancer.	56	91%
Information about response rates is important to most patients with advanced cancer.	56	89%
This section would be too upsetting to most patients.	57	9%

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Toolkit as a whole

	Number of respondents	Percent who responded "agree" or "strongly agree"
This informed consent tool would help most patients to make more informed treatment choices.	38	87%
This informed consent tool would be useful to most patients.	41	98%

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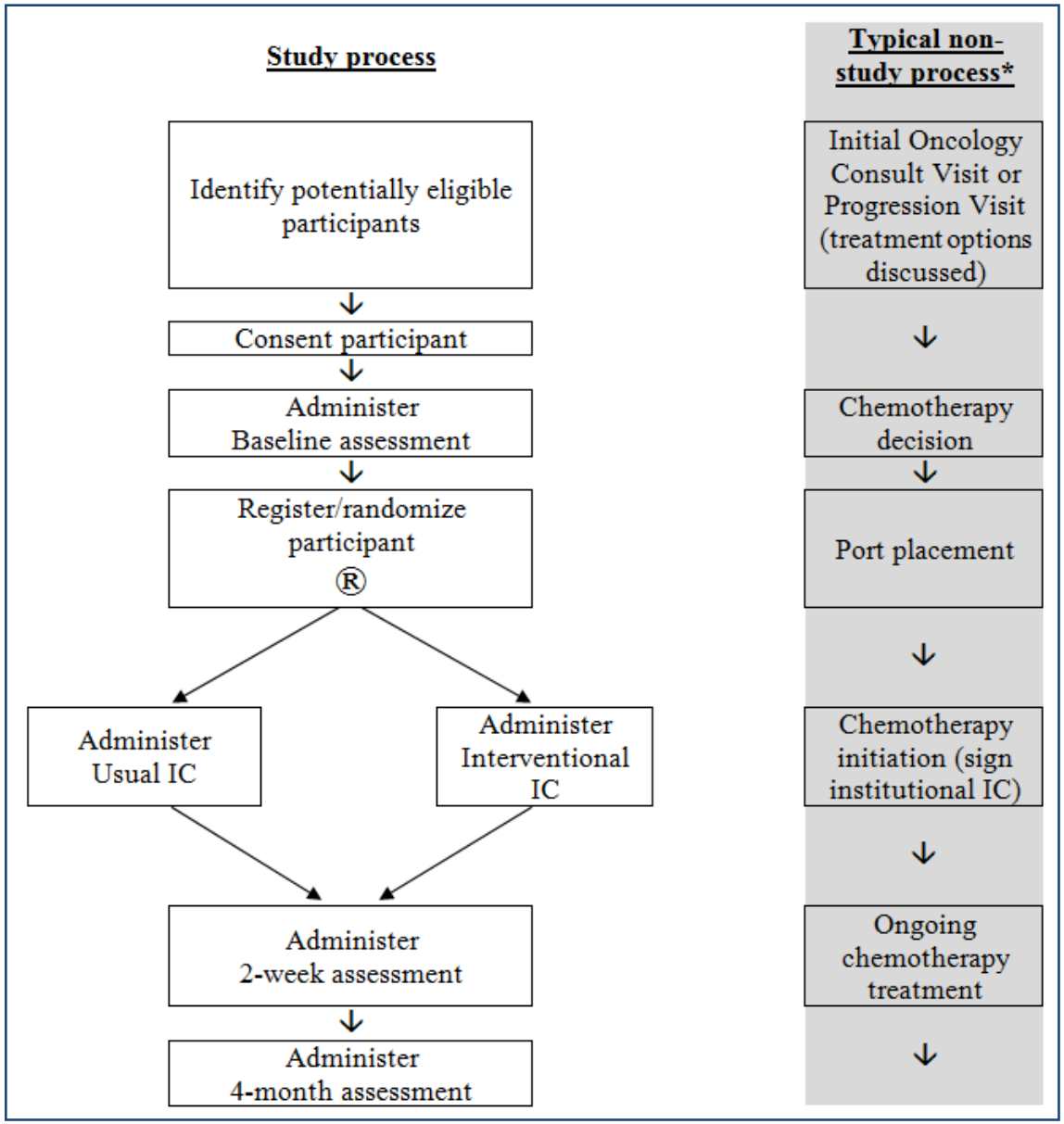
Part 3: RCT



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Multi-site:
Thanks to Alliance Funding

- RCT accruing at:
  - Dana-Farber Cancer Institute
    - Dana-Farber Milford
    - Dana-Farber South Shore
  - University of San Francisco
  - University of North Carolina
  - Virginia Commonwealth University
  - Novant Health, North Carolina

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RCT Study Process

1. Identify potentially eligible participants
2. Consent participant for research
3. Administer baseline assessment
4. Register/ randomize participant
5. Administer intervention (usual IC or investigational IC)
6. Administer 2-week assessment
7. Administer 4-month assessment
   - $25 gift card will be given at the completion of the 4-month assessment

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Outcomes

- Understanding of the risks and benefits of palliative chemotherapy
- Decisional conflict

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Meanwhile…

- Just now embarking upon a new project to…

- **Adapt** this suite of chemotherapy informed consent (IC) videos and booklets to meet the needs of a) English-proficient and b) Spanish-proficient **Latinos** with advanced GI cancers and their caregivers.

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Rationale

- Latinos are the largest minority population in the US, yet communication inequalities remain a significant obstacle to treatment decisions and quality care across the cancer continuum.

- In a recent study of 1194 patients with metastatic cancer we found that Latinos were far less likely than Whites to understand that chemotherapy was non-curative (OR 0.35, $p<0.01$). [Schrag, NEJM]

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Overview of Study Design

- Adapt existing IC tools through a four-phase qualitative research process of:
  1. key stakeholder engagement
  2. focus groups
  3. stakeholder-driven revisions
  4. cognitive interviews

- Multicenter randomized trial of intervention involving 116 Latinos with advanced colorectal or pancreatic cancer and their caregivers, recruited from 7 academic and community cancer centers serving diverse Latino populations across the US.

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Suggestions?

- Best ways to proceed with both the parent study and the new study?

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