Fall 2020 SWOG ONCOLOGY RESEARCH PROFESSIONALS OPEN FORUM B Meeting – Virtual

SUMMARY

Date: Thursday, September 24, 2020
Time: 2:15 – 3:15 pm CT

Agenda:

Welcome

Study Participant Follow-up Documentation with Q&A

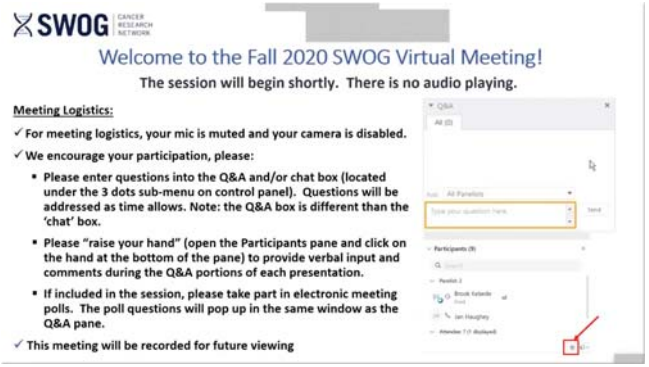
Cancer Progress with Q&A

Conclusion and Evaluation Poll

Welcome
0:00:00
Stefanie Parker thanked attendees for tuning in.

- Noted two ORP open forums: this is Open Forum B
- Recordings and slides will be posted to website
- Two presentations, each about 20–24 minutes, followed by Q&A
- Those with questions should save them until the "Questions" slide appears
- Can then raise their hand and IT team will unmute

- Parker said first presentation would be "Study Participant Follow-up Documentation."
- Second would be "Cancer Progress"
- Poll at the end of the forum for attendees to complete
- Helps them determine what topics people want to see at next open forum



0:01:23
Parker presented the agenda.

0:01:37
Parker introduced speakers for first presentation:

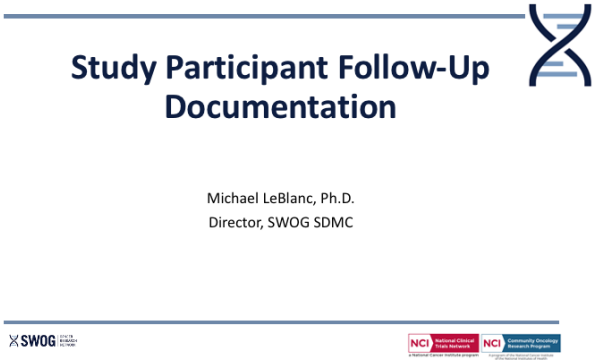
- Mike LeBlanc, group statistician and director of SWOG Statistics and Data Management Center in Seattle
- Phyllis Goodman, SWOG Statistical Center in Seattle

Study Participant Follow-up Documentation with Q&A

0:02:04

LeBlanc said he loves to talk about data.

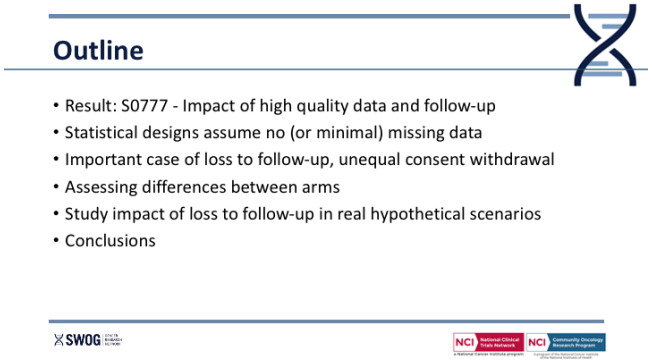
- Would discuss importance of study follow-up in understanding trial results



0:02:31

LeBlanc presented outline:

- When it goes right:
  - High-quality statistical design
  - Great follow-up data
  - SWOG S0777 myeloma study of several years ago
- What statistical design got us there:
  - How it depends on having minimal follow-up data beyond the construct of design itself
- Will discuss couple of important cases of missing data
  - Lost to follow-up
  - Unequal consent withdrawal
  - Even greater impact if these have differences between arms
- Some hypotheticals
- Conclusions

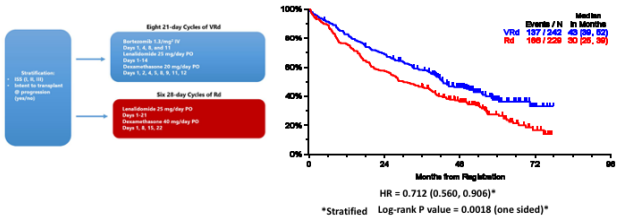


0:03:33

SWOG S0777

- Antje Hoering was study statistician
- Results had huge impact
  - Used for regulatory extensions
  - Presented at Oishi Symposium
- Study schema
  - Randomized to 3 drugs vs 2 drugs
- Blue line corresponds to 3-drug progression-free survival
  - Above the red curve
- Statistics at bottom of slide
  - Small p value, meaning strongly significant result
  - Hazard ratio to represent treatment effect
    - Smaller hazard ratio means much more positive treatment effect
- LeBlanc said the only reason these indicators are meaningful is because SWOG had good follow-up data
  - And equal follow-up data across arms
- Wants everyone to understand what a survival curve means
  - Looking at 24 months
    - On control arm roughly 55% PFS
    - On treatment arm about 65% to 70%

SWOG Myeloma Study S0777 Presented in Oishi Symposium Fall 2017. Key role of the CRAs in achieving high quality follow-up data and results



0:05:05
Statistical design

- Sample size assuming about 110 patients per year
  - 440 overall over 4 years
- Median PFS for control group of about 3 years
- Exponential survival distribution
- Roughly 2.5 years of follow-up
  - Needed to assume would have good follow-up for at least 2.5 years
- Statistical power shown
- Conclusions depend on patient follow-up

Statistical Design of S0777

- The sample size was based on the assumption of an eligible patient accrual rate of 110 patients per year (440 eligible patients over 4 years), a median progression-free(PFS) survival of about 3 years in the control group, exponential distribution of progression-free survival, and roughly 2.5 years of additional follow-up
- The study was designed to detect a hazard ratio of 1.5, with approximately 87% power and an overall study alpha of 0.05
- Conclusions depend on complete patient follow-up (on both arms)

SWOG

0:05:47
Critical elements in evaluating therapeutic interventions

- As we move through phase 1, 2, and 3, initially
  - Biologic activity
  - Need to understand safety and toxicity
- Later on need to understand
  - Clinical efficacy
    - Clinical response
    - Patient-reported outcomes in some settings
    - Disease recurrence or progression
    - Progression-free survival
    - Overall survival
- Other long-term events
- Latter items in particular mean we need to follow patients equally on both arms over time

Critical Elements in Evaluating Therapeutic Interventions

- Biological Activity
- Safety/Toxicity
- Clinical Efficacy
  - Clinical Response
  - Patient Reported Outcomes
  - Disease recurrence or progression
  - Survival
- Other long-term data
  - Long term adverse events and related malignancies

SWOG

0:06:26

What can go wrong?

- LeBlanc said statisticians often care about two things:
  - Bias
  - Variance
- What bias means:
  - Tendency for statistical result to differ on average from true state of affairs because of flaws in
    - Study design
    - Study conduct
    - Study data
  - Bias can result from loss to follow-up, because loss or consent withdrawal may be related to underlying health status
    - Lost patient may be doing worse (or better) than comparable patient with complete data
    - Statistician doesn't know what to do with this because we don't know nature of bias
      - Direction of it
      - How to model it
    - No good statistical solution to eliminate this problem

Bias and Missing Follow-up Patient Data

- A tendency for a statistical result to differ on average from the true state of affairs, often due to flaws in the design or conduct of a study
- Lost to follow-up, can introduce bias because the reason for the loss, or consent withdrawal "MAY" be related to the underlying patient health status
- A lost patient maybe doing worse (or better) than a comparable patient with complete data
- Worse yet – we don't know the nature of the bias
- Leads to either incorrect or less impactful statistical results

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0:07:33

Looking at cases

- He does this in clinical trials training course from time to time
- Patient A, treatment 1
  - Registration March 1
  - Assessment May 1
  - Another assessment July 1
  - Progression Oct 1
- Patient B, treatment 2
  - Registration March 1 (typo)
  - Assessment May 1

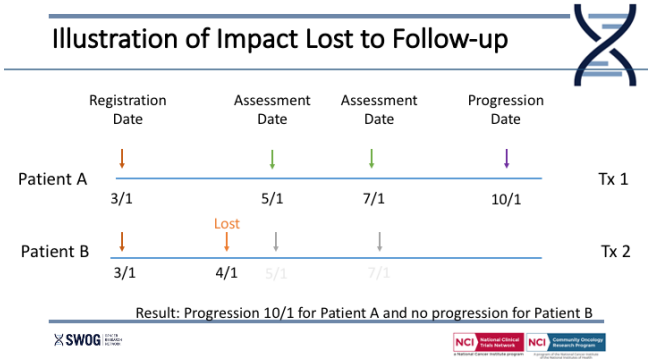
Illustration of Impact Lost to Follow-up

Result: Progression 10/1 for Patient A and 7/1 for Patient B

- Progression July 1

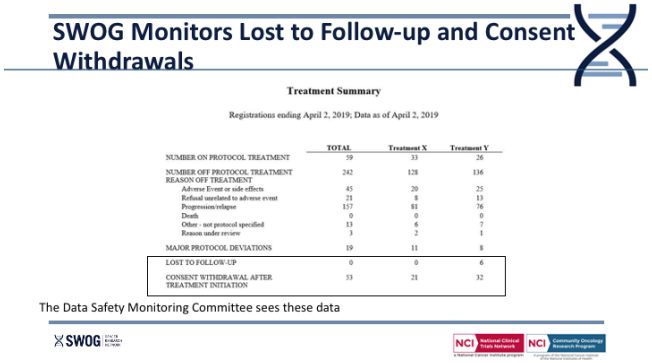
0:08:49

- What happens if we collected data slightly differently?
  - And lost patient on March 1 (still progressed July 1)
  - Result would have been a progression for patient A but none for patient B
- So a different conclusion



0:09:10

- Seeing this happen on both arms, of course
- LeBlanc said attendees might recognize top part of slide, but they don't see the bottom part
  - Only the Data and Safety Monitoring Committee and statisticians see that
- More loss to follow-up on treatment Y than X
- More consent withdrawals on treatment Y too
- Would lead one to potentially incorrect conclusions in comparing treatments X and Y



	TOTAL	Treatment X	Treatment Y
NUMBER ON PROTOCOL TREATMENT	59	33	26
NUMBER OFF PROTOCOL TREATMENT	242	128	136
REASON OFF TREATMENT			
Adverse Event or side effects	45	20	25
Refusal unrelated to adverse event	21	8	13
Progression/relapse	157	81	76
Death	0	0	0
Other - not protocol specified	13	6	7
Reason under review	3	2	1
MAJOR PROTOCOL DEVIATIONS	19	11	8
LOST TO FOLLOW-UP	0	0	6
CONSENT WITHDRAWAL AFTER TREATMENT INITIATION	53	21	32

0:09:52

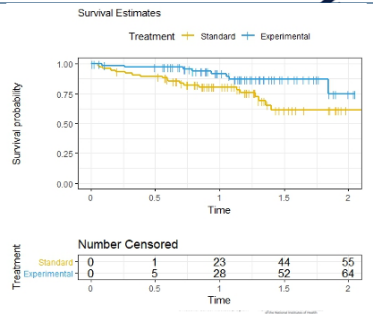
Another example

- SWOG study SXXXX
- Actively accruing
- Has accrued about 1/3 of patients
- Survival curves
  - Blue line of experimental arm looks promising
    - Above beige line
- If this was phase 2/3 study and we were looking at this data in the middle
  - P value .01
  - Looks like a positive phase 2 that should carry on to phase 3
- To clarify, the blue curve is higher because proportion of people surviving on experimental arm is greater

Study SXXXX (actively accruing)

- Study accrued 1/3 patients
- Survival curves look promising
- A Phase II analysis of data yields significant result

  p-value=.01 (one-sided)



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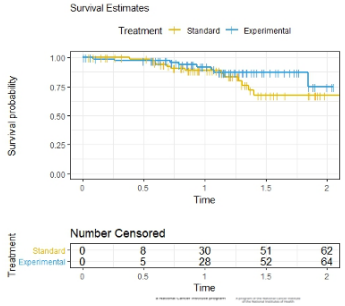
What if?

- Same study
- Accrued 1/3 of patients
- But now differential follow-up
- LeBlanc said he used same data but he hypothetically lost 6 patients to follow-up
- Now curves are not very promising
- If this were a phase 2/3 study, p value would have been .12
- So might not have carried on with phase 3 portion of study
- 6 patients changed results of what would have been seen as a positive study
- Data is unstable early on when representing a few patients, so bad things can have a big impact

Study SXXXX (actively accruing)

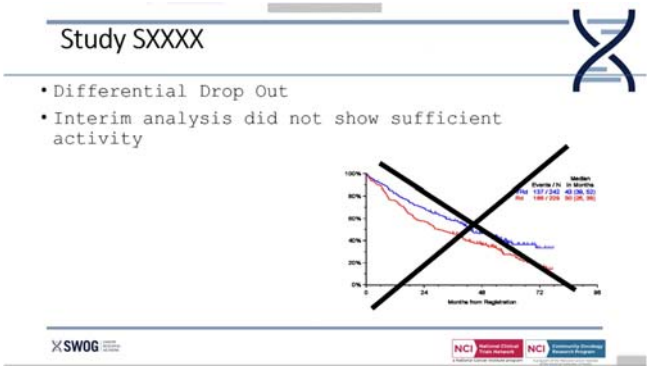
- Study accrued 1/3 patients
- But now assume there is differential lost to follow
- 6 patients on Standard arm, 0 on Experimental arm lost
- Conclusion: early results not very promising
- If a Phase II/III study maybe close study for accrual

  p =.12 (one-sided)



0:11:40
Study SXXXX

- Differential dropout on this hypothetical study would have meant we didn't finish the results



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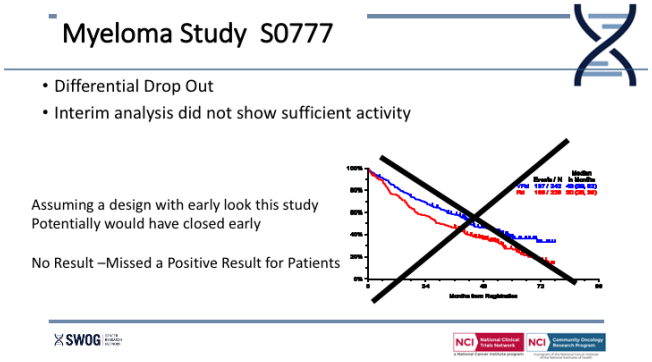
Myeloma study S0777

- But the hypothetical study was first few patients on S0777
- Wasn't phase 2/3 design, but if it had been and we had had that differential follow-up as opposed to the good follow-up we did have on that study, we may have never gotten the positive result we saw in that study, just because small amount of data wasn't coming in appropriately



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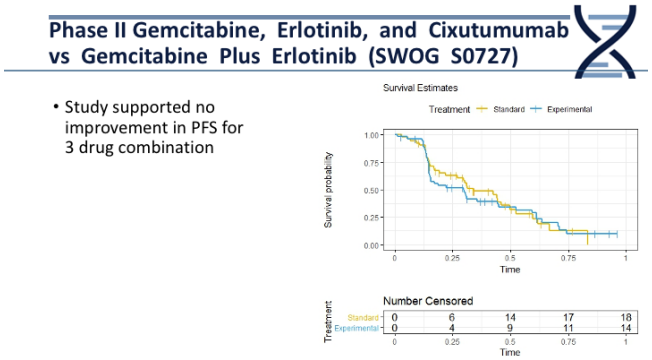
Another example

- SWOG randomized phase 2
- Study supported no improvement in PFS for this 3-drug combo compared to the 2
- Standard looks slightly better than experimental, but they're pretty close

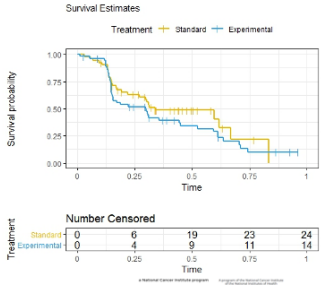


0:12:37

- LeBlanc said he did the same trick here
  - Introduced hypothetical dropout of 6 patients
  - See experimental arm looks harmful
  - Study did not go forward, but could cause significant interpretation problems and safety issues had we had differential follow-up
- Affects both phase 2 and phase 3 studies

Phase II Gemcitabine, Erlotinib, and Cixutumumab vs Gemcitabine Plus Erlotinib (SWOG S0727)

- Hypothetical differential loss to follow-up
- Could have led to conclusion of harm for experimental arm
- Significant implications for study conduct



0:13:12

Conclusions

- Complete patient follow-up and minimizing the impact of consent withdrawal is critical for interpretation by statisticians and clinicians
- Absolutely essential in terms of data monitoring and decision-making as well
  - Not just for the final analysis but also for decisions made on the fly
  - Every randomized phase 2 study is sent to DSMC every 6 months
    - So decisions being made on relatively small numbers of patients
    - Have to get this right
- No statistical adjustments for this issue
- Practical issues will be addressed by Phyllis Goodman

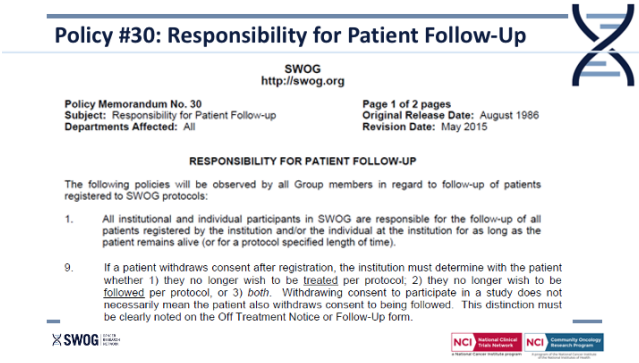
Conclusions

- Complete patient follow-up and minimizing the impact of consent withdrawal is critical for study interpretation
- Follow-up on every patient is essential for both final statistical analysis but also for trial monitoring and decision making. Important decisions are made on small numbers of patients
- There are no statistical adjustments that correct for this issue
- Practical steps – focusing on Lost to Follow-Up and Consent Withdrawal

0:13:54
Goodman presented on policy and implementation.

0:14:05
Policy 30

- Implementation is what is in SWOG policy 30: responsibility for patient follow-up
- Goodman said she would focus on two points:
  - Item 1
  - Item 9



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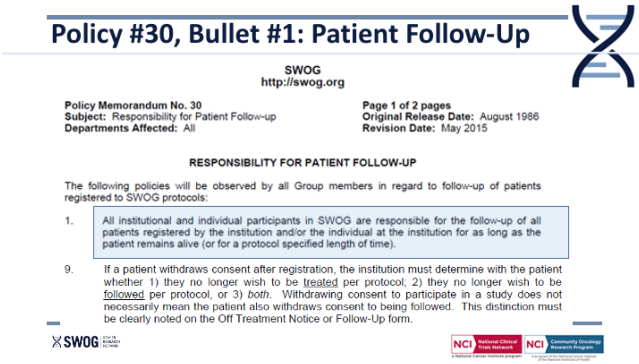
Item 1

- All institutional and individual participants in SWOG are responsible for the follow-up of all patients registered for as long as the patient remains alive or as specified in the protocol



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- Important to understand how follow-up is calculated
- Use last contact date
  - Which is last date patient was known to be alive
- For newer studies, comes from Vital Status Form
- For older studies, gleaned from any visit with a contact date
- Follow-up schedule and total length expected is both protocol-specific and treatment status-specific
  - Can be short as a month
  - Typically every treatment cycle during treatment
    - Every 6 or 12 months after treatment
- Check the protocol
- Follow-up is considered delinquent if expected update is more than 60 days overdue

Vital Status Updates/Follow-Up

- Last contact date is the date the patient was last known to be alive
  - From either the Vital Status Form (newer studies), or other form with a visit/contact date

- Follow-up schedule is protocol- and treatment status-specific
  - Could be as short as monthly or as long as annually
- A patient's follow-up is delinquent if update to their last contact date is more than 60 days overdue

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0:15:25

Patients you can't find

- Patient registered to trial, but now can't find them
  - Don't respond to calls
  - Don't attend appointments
- Procedure to declare patient "lost to follow-up"
- Both criteria must be met:
  - Last contact date must be more than 2 years ago
  - Since that last contact, you must have at least 3 documented phone attempts to contact patient or one certified letter to last known address that is returned or not answered
- Until then, patient will continue to appear on expectation report

What about that patient I can't find?

- To declare a patient "Lost to Follow-Up" both of the following criteria must be met
  - The last contact date (date patient last known to be alive) must be more than 2 years ago
  - Since the last contact, there are either (a) at least 3 documented phone attempts to contact the patient or (b) one certified letter to the last known address that was either returned or not answered

And yes, this means this patient will continue to show up on your expectation report until they are either found or the above criteria are met and the form completed.

0:16:08
Expectations

- Show up in report in couple of ways
- For studies that use Vital Status Form:
  - Show up same as other dynamic expectations
    - With “period beginning” in description (top of slide)
- For studies not using this form:
  - Can show up as form overdue
- For studies where follow-up is just follow-up form:
  - When patient is overdue, shows up as “follow-up”

Vital Status Updates/Follow-Up Expectations

- A specific form required to update Last Contact date, Vital Status or any of the other “dynamic” expectations

SWOG Patient ID	Expectation	Days Overdue	IPR
275285	Off Treatment Vital Status Form/Period beginning 09/20/2019	181	FORM/FUP
277517	On Treatment Vital Status Form/Period beginning 04/15/2020	65	FORM/FUP
	Adverse Event Form/Period beginning 04/15/2020	65	FORM/FUP

- For patients who are Off Treatment and only the Follow-Up form is overdue

SWOG Patient ID	Expectation	Days Overdue	IPR
705316	Follow-up	78	FUP
265017	Follow-up	293	FUP

SWOG

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0:16:43
IPR criteria

- Site’s performance out of compliance if >15% of patients overdue on this measure
- Recognize sites can do only so much
  - Always be some patients who are difficult and can’t be found
  - That’s why compliance level is 15% and not 0%
- If just 1 or 2 patients on your report, won’t matter for compliance
- Level applies overall to data management sites or top-level sites
- These sites will see rates for all affiliates
- But only overall level for LAPS or NCORP is used for determining compliance
- SWOG’s overall delinquency rate on Sept 2 was 7.4%
- 15 data management sites were over limit

Institution Performance Review Criteria – Vital Status Updates/Follow-Up

- A site’s performance is out of compliance if greater than 15% of their patients are overdue on this measure
  - Recognize that sites only have so much that they can do to get follow-up on a subset of patients that may be very difficult
  - 15% overall at the Data Management (top-level) institution
  - Overall, for SWOG, as of September 2, 2020
    - The delinquency rate was 1006/13,687=7.4%
    - 15 Data Management institutions were over the limit

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0:17:34

Withdrawal of consent is next piece of policy:

- If a patient withdraws consent after registration, the institution must determine whether the patient
  - 1) no longer wishes to be *treated* per protocol
  - 2) no longer wishes to be *followed* per protocol
  - 3) both
- Withdrawing consent to participate in study does not necessarily mean they withdraw consent to be followed

Policy #30 Bullet #9: Withdrawal of Consent

SWOG
http://swog.org

Policy Memorandum No. 30
Subject: Responsibility for Patient Follow-up
Departments Affected: All

Page 1 of 2 pages
Original Release Date: August 1986
Revision Date: May 2015

RESPONSIBILITY FOR PATIENT FOLLOW-UP

The following policies will be observed by all Group members in regard to follow-up of patients registered to SWOG protocols:

1. All institutional and individual participants in SWOG are responsible for the follow-up of all patients registered by the institution and/or the individual at the institution for as long as the patient remains alive (or for a protocol specified length of time).

9. If a patient withdraws consent after registration, the institution must determine with the patient whether 1) they no longer wish to be treated per protocol; 2) they no longer wish to be followed per protocol, or 3) *both*. Withdrawing consent to participate in a study does not necessarily mean the patient also withdraws consent to being followed. This distinction must be clearly noted on the Off Treatment Notice or Follow-Up form.

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0:18:01

From presentation by Keisha Humphries, former ORP chair:

- Presented at 2019 Oishi Symposium
- Goodman encouraged all to listen to her presentation
  - Found on swog.org
- Understand what patient is saying
  - Refusing further treatment and testing?
  - Refusing any follow-up, including indirect?
- Follow-up at minimal acceptable level is updating survival status and last known date alive

From Keisha Humphries, former ORP Chair

- Need to be able to understand what the patient is saying. Is the patient
  - Refusing further treatment, additional tests, etc.
  - Refusing continuation of <u>any</u> follow-up
- Follow-up is, at a minimal acceptable level, the updating of survival status and date of last contact

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0:18:34

- Humphries emphasized need for conversation with patient to understand why they don't want to participate
  - Don't want more imaging? Bone marrow biopsy coming up? Uncomfortable with someone on study team?
  - Are there options?
    - Allow at least minimal follow-up status (i.e., survival status)?

From Keisha Humphries, former ORP Chair (con't)

- Have a conversation with the patient to understand why they no longer want to participate
  - What are the particular concerns. Is there particular procedure that they don't like? Or maybe they just don't feel comfortable with a specific doctor or study team member?
  - Are there solutions to allow at least minimal follow-up. Are there alternative options for this patient?

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0:19:07

Withdrawal of consent form

- If you're certain patient wants no future follow-up, withdrawal of consent form available for Rave studies by request from study team or data coordinator
- Will be asked to upload source documents that determine that withdrawal
- Data coordinator at SDMC will review form and source documents
    - To confirm withdrawal was patient-initiated, not site assuming patient wanted to withdraw
- Goodman said withdrawals should be vetted through site head CRA or other site leadership
- Can also consult data coordinator
- Formal withdrawal should not be used by sites to stop following patients

Withdrawal of Consent Form

- Rave Studies
  - Available by request to the Study Team at the SDMC
  - Source documents required to support the determination of a withdrawal
- During the review by the Study Team
  - Looking to see that the withdrawal was patient initiated, a site can not assume patient's intent
- Should be vetted through Head CRA and/or site leadership as well as Data Coordinator at SDMC
- Not a tool to be used by study sites to stop following patients

SWOG

0:19:59

Outstanding expectations and queries after withdrawal

- Any form or report due prior to date of consent is still due
- Includes any expectations with "Reporting period begins" date prior to withdrawal and any specimen
- As with any other specimen, if it wasn't collected, use "Notify that a Specimen Cannot Be Submitted" function on Specimen Tracking
- Any query by a data coordinator or any system query from Rave must be responded to

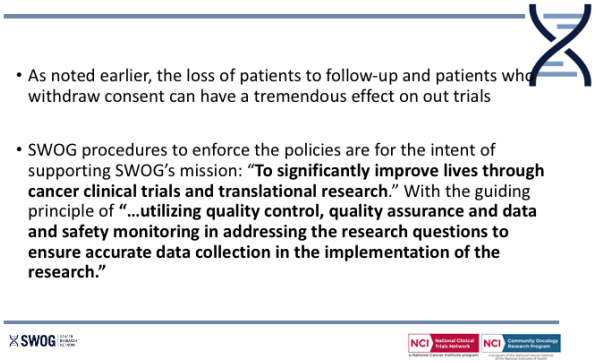
Withdrawal of Consent – Outstanding Expectations and Queries

- Any form/report due prior to the date of withdrawal of consent is still due
  - Any expectations with a "Reporting period begin" date prior to the withdrawal is still due
- Any specimen due prior to the date of withdrawal of consent is still due
  - Baseline specimens as well as post-baseline specimens
  - If it wasn't collected use the "Notify that a Specimen Can Not be Submitted" function on Specimen Tracking
- Any query requesting clarification on treatment prior to withdrawal still needs to be responded to

SWOG

0:20:43

- Loss of patients to a study, from loss to follow-up or withdrawal of consent, can have tremendous negative effects on a trial
- Want to run best trials we can
- SWOG procedures are set out to support SWOG's mission (see slide)
- Goodman said all need to work together to achieve these goals



0:21:33
Goodman hoped by 2022, when meeting is scheduled for Seattle, members can visit Olympic National Park

- Photos in slide are from Goodman's trip there last summer

0:22:05
Parker opened floor to questions.

Parker noted comprehensiveness of LeBlanc's and Goodman's presentations could be reason for lack of questions.

Annette Betley asked how they are handling patients they are unable to locate because of COVID? Attempted to make phone calls, contact PCPs, etc. Attempts have been made. Should sites continue to do it same way? Or fill out lost to follow-up form?

- Goodman said they have not discussed specific implications of effects of COVID and what they will change

- At this point, follow same procedure
- Keep documenting that you've tried
- At 2-year time point, can submit form
- LeBlanc said if she knows there's a COVID-related issue re deviations, fill out COVID data collection form
- Betley confirmed they've been doing that
- Goodman said they're looking at institutional performance measures and she can see follow-up is becoming more of an issue
- Will have to think about it at policy level

Parker said questions could also be added to Chat. They would be posted with answers to SWOG website.

0:25:28
Parker introduce Kristine Abueg, oncology clinical trials research nurse for Kaiser Permanente in Roseville, CA.

- Also member of SWOG ORP executive committee
- Will discuss cancer progress and types and categories of oncology treatment

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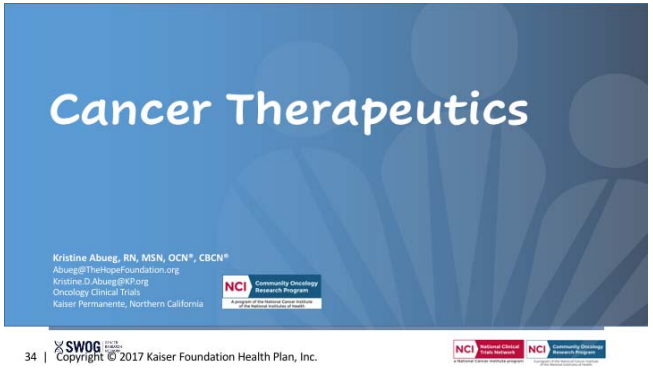
Cancer Progress with Q&A

0:25:58

Abueg said she is based at NCORP in northern California near Sacramento.

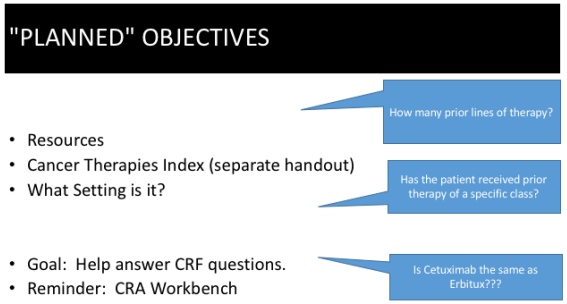
- Noted audience could also email her with follow-up questions from Oishi Symposium
- Talk on cancer therapeutics is designed to help answer some of the questions that come up with CRFs related to therapies



0:27:23

Planned objectives

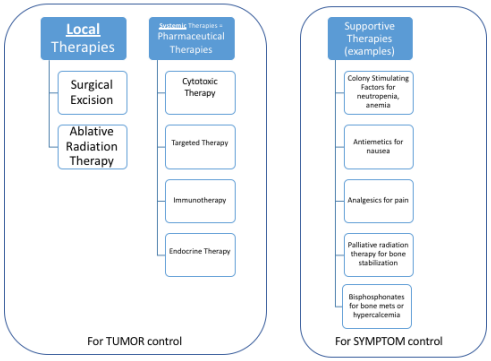
- Talk about some of the resources she will recommend for completing CRFs
- Created a cancer therapies index
- Will also discuss how to decipher which treatment a prior therapy was given in
- "Planned" objectives, but also wants to remain true to "open" of Open Forum
- Open Forum when face-to-face is more like office hours
- Session is to help with CRF questions she is often asked about



0:28:57

Cancer therapies

- Abueg gave an example CRF question:
  - Was prior therapy patient had in local control or systemic therapy or symptom control?
  - Two broad categories of therapies:
    - Symptom control, shown on right in slide
    - Tumor control, at left
  - Said focus today would be on tumor control group
  - Tumor control breaks into 2 categories:
    - Local therapies



- Surgical excision
- Ablative radiation therapy
- Exert influence on immediate area around tumor

▪ Systemic therapies
- Move through entire body
  - Sometimes crossing blood–brain barrier
- Typically drugs

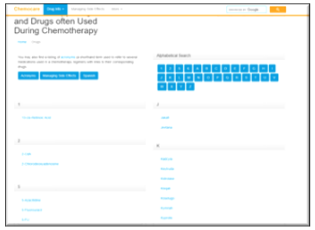
0:30:09

- Abueg started with resources
- Recommended several good vetted sites

- chemocare.com
  - Initiative by Cleveland Clinic
  - Indexed cancer therapies
  - Enter name of drug
  - Get patient education sheet
    - Brief indication of drug, side effects profile, etc.
  - Often useful when working with treatments in standard of care arm
  - Site includes index of treatment regimen abbreviations
    - E.g., details on ABVD, FOLFOX, etc.
    - Not as detailed as descriptions of individual drugs

RESOURCES: WWW.CHEMOCARE.COM

http://chemocare.com/chemotherapy/drug-info/default.aspx

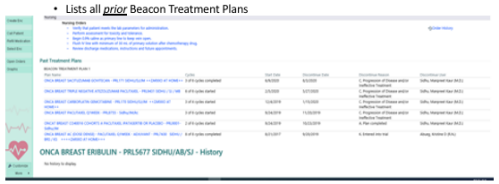


0:32:13

- BEACON
  - Epic chemo portal
  - If you scroll to very bottom, lists all prior BEACON plans for that patient
    - Which drugs
    - Regimen start date
  - Caveat
    - Ignore the discontinue date, as it is not last dose
    - It's date physician ended the plan in BEACON
    - Could be years after last physical dose
  - But it's a good source to check what patient was previously on

Resources: BEACON plan history [Epic users]

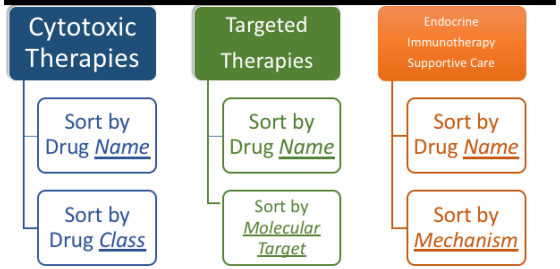
- EPIC
  - Current BEACON plan
    - Scroll to BOTTOM
      - Lists all *prior* Beacon Treatment Plans



0:33:21

- Abueg created a handout resource
  - Accessible on virtual meeting website for this session under "handouts" (https://webcast.imsts.com/SWOG-Thurs-ORP-Open-Forum-Session-B)
  - Handout is a searchable index in PDF of all approved cytotoxic and targeted therapies, endocrine therapies, and immune therapies

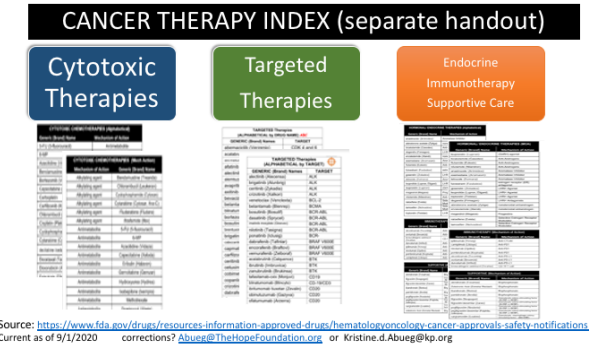
CANCER THERAPY INDEX (separate handout)



Source: https://www.fda.gov/drugs/resources-information-approved-drugs/hematologyoncology-cancer-approvals-safety-notifications
Current as of 9/1/2020 corrections? Kristine.d.Abueg@kp.org

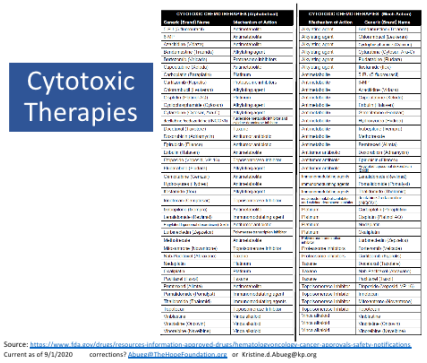
0:33:59

- Abueg displayed a screenshot with index pages
- First is cytotoxic therapies
- Next page is targeted therapies
- Then endocrine therapies
- Immune therapies
- Supportive care therapies
- Abueg said she created the index based on the FDA.gov approval list
- Confirmed its accuracy as of Sept 21, 2020
  - Please email her any corrections



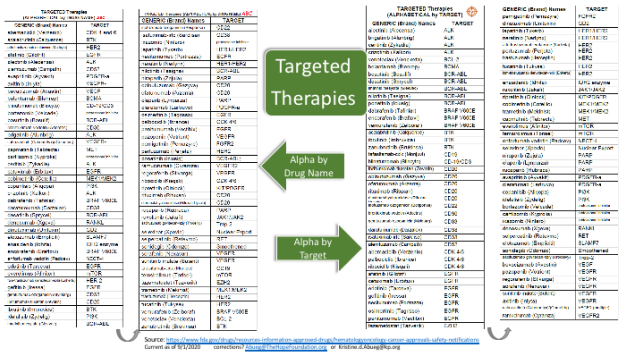
0:34:57

- Cytotoxic therapies page
- Has two tables
  - Identical content, ordered differently
- Table at left is alpha order by drug name
  - Brand name and generic name
  - Also drug class
- Table at right reorders same information by class
  - Groups antimetabolites, platinums, e.g.
- Makes it searchable and easier



0:35:59

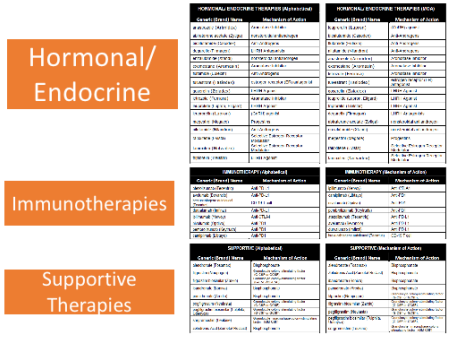
- Done the same with targeted therapies
- But more than can fit on a page
- Abueg said she did this session at SWOG's fall 2019 meeting
  - 77 targeted therapies then
  - 86 now
- Alpha index flows over to next column
  - Generic name
  - Brand name in parentheses
  - Then correlating target



- Next page takes same list and reorganizes it by target
  - Alpha inhibitors together, CD20 inhibitors, VEGF inhibitors, etc.
  - Done for easy reference

0:37:12

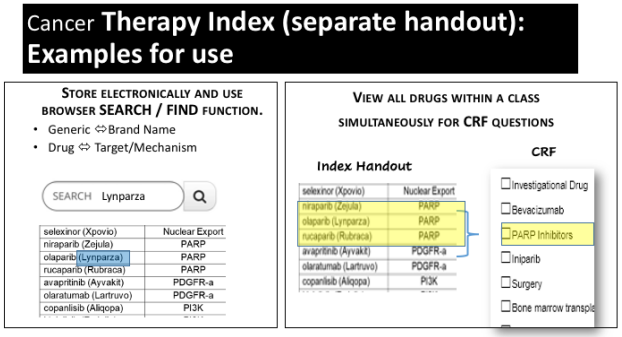
- Third category is hormonal endocrine therapies
- Left column alpha with correlating mechanism of action
- Right column is grouped by mechanism of action
- Below that are immunotherapies
  - Limited to checkpoint inhibitors
    - Anti-PD-1, anti-PD-L1, anti-CTLA4
  - One CD19 T-cell therapy
  - Did not include CAR-T therapies
- At bottom are supportive therapies that tend to be most commonly asked about on case report forms
  - E.g., prior bisphosphonates, GMCSF, GCSF, etc.



0:38:21

Abueg turned to ways to use this information.

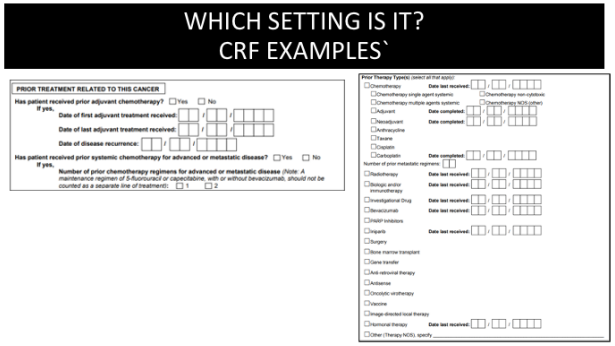
- Suggests make it searchable document
- E.g., when physician refers to Lynparza, search it
  - Generic name is olaparib and it's a PARP inhibitor
- Another use is to view all drugs in a particular class for answering CRF questions
  - E.g., CRF may ask has patient been on PARP inhibitors
  - Look at group in document and compare against medical record
- Abueg welcomed suggestions as to whether tool is useful and how to make it better



0:40:00

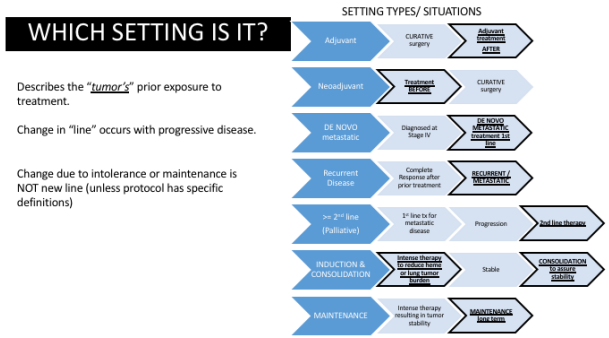
Abueg turned to CRF questions about “setting”

- Which setting is it?
- Slide presents two examples
- At left is on-study CRF for colon cancer
    - Asks how many prior lines of systemic therapy for advanced or metastatic disease
- At right is entry CRF for breast cancer study
- How do you know what setting a prior therapy was given in?



0:41:00

- Setting is analogous to terms first line, second line, third line
- Major setting categories:
    - Adjuvant
        - After a patient has had curative surgery, typically
        - No evidence of disease, but do cleanup
        - Or adjuvant in addition to curative therapy to reduce risk of micrometastases
    - Neoadjuvant is treatment before curative treatment to minimize risk of metastases
        - For breast cancer in particular, neoadjuvant therapy is to assure a curative surgery
            - Assuring ability to get clean margins
            - Reducing a mastectomy to a lumpectomy
    - De novo metastatic disease
        - Situation of patient diagnosed at stage 4
            - E.g., patient diagnosed with colon cancer and screening CT finds metastases
            - First treatment given is considered first line
            - Term first line usually reserved for metastatic treatment
    - Recurrent disease different from de novo metastatic but often considered first line therapy



        - Patient got therapy, had complete response, and for a time they were no evidence of disease (NED)
            - Then tumor recurred in a metastatic or local setting
            - Treatment still considered first line
    - Second line therapy
        - Patient has had first line therapy and progressed on therapy
        - Next course of treatment is second line
    - Induction and consolidation usually used in hematological malignancies and in lung cancer
        - Induction is intensive therapy to reduce tumor burden
        - Then achieve a level of stability: stable disease or response
        - Then get consolidation to assure stability
    - Maintenance therapy follows intensive therapy to ensure tumor stability
        - Then to maintain them in long-term setting
        - Done in myeloma or lung cancer
        - Not switching to maintenance because of progression, but move to longer-term therapy
- Change in tumor setting refers to tumor's prior exposure to treatment
- Change in line, from first to second, e.g., occurs with progression
    - E.g., patient going from first line disease and becomes intolerant of their treatment
        - E.g., neuropathy or rash
    - … but not tumor progression, don't call it change in line
    - Look at CRFs and protocols to see what they specify

0:45:52
Abueg invited questions about previous slides.

Said has interactive case studies to demonstrate settings.

- Will post interactive questions
- Can answer them in Chat

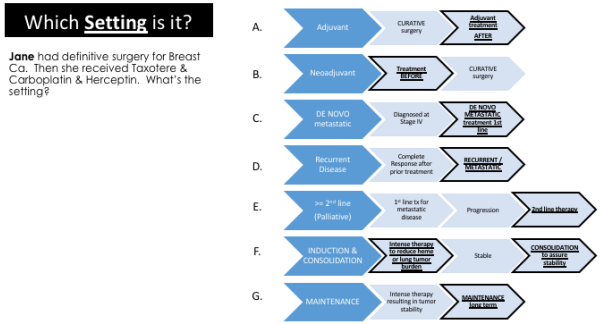
Interactive!

Consider each of the following patient cases.

For each, what is the correct "treatment setting"?

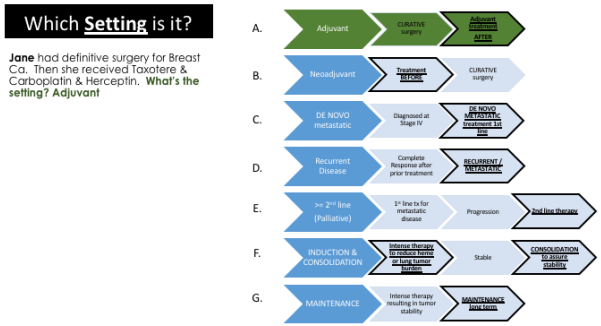
0:46:42
Which setting is it?

- Jane had definitive surgery for breast cancer. Then she received taxotere and carboplatin and Herceptin. What is the setting?



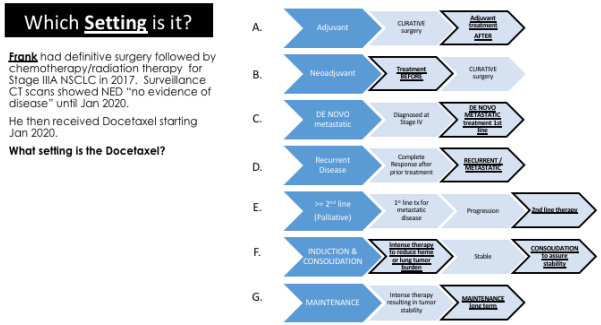
0:47:20

- Setting would be considered adjuvant
- The treatments given after definitive surgery are considered adjuvant therapy



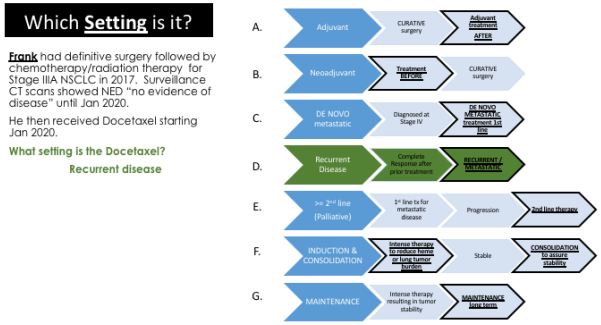
0:47:31

- Frank had definitive surgery followed by chemotherapy and radiation therapy for stage 3a non-small-cell lung cancer in 2017. Surveillance scans showed he was NED no evidence of disease until January 2020. Then prescribed docetaxel. What is the setting of the docetaxel?



0:48:27

- This setting is considered recurrent disease because he had a period of complete response and then he recurred 3 years later. Docetaxel is the first line in a recurrent setting.



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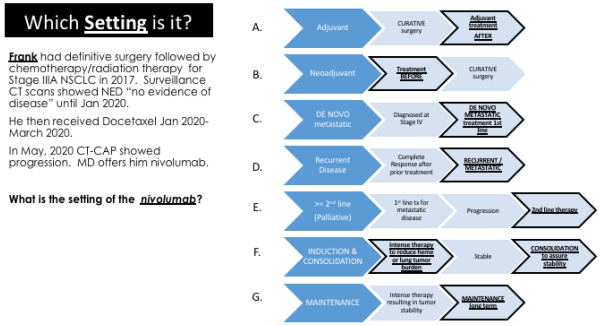
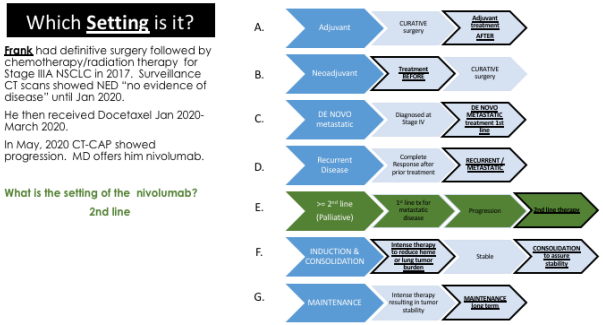
- Still with Frank. Received docetaxel from Jan to Mar 2020. In May 2020, CT-CAP showed progression. MD offers him nivolumab. What is setting of nivolumab?



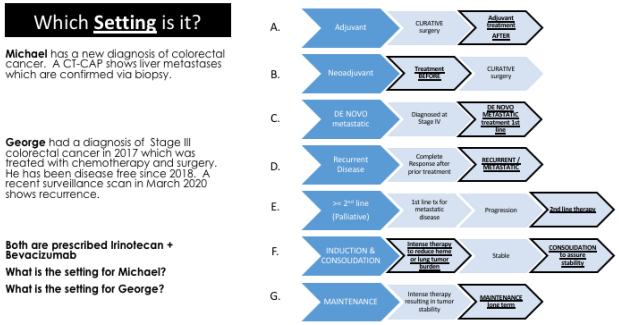
0:49:20

- Setting is second line after docetaxel, which was first line.



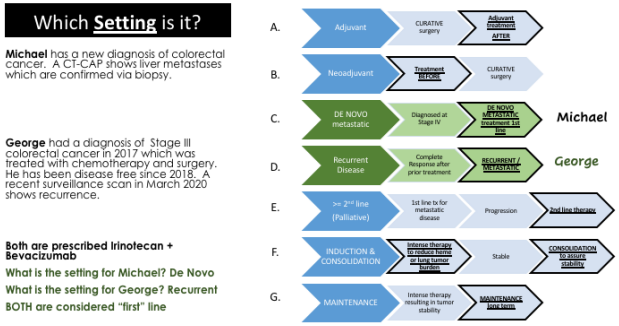
0:49:36

- 2 patients here. Michael as a new diagnosis of colorectal cancer. A CT-CAP at diagnosis shows liver metastases, which are confirmed via biopsy.
- George diagnosed with stage 3 colorectal cancer in 2017, which was treated with chemo and surgery. Been disease free since 2018. Surveillance scan in March 2020 showed recurrence.
- Both prescribed irinotecan and bevacizumab. What settings?



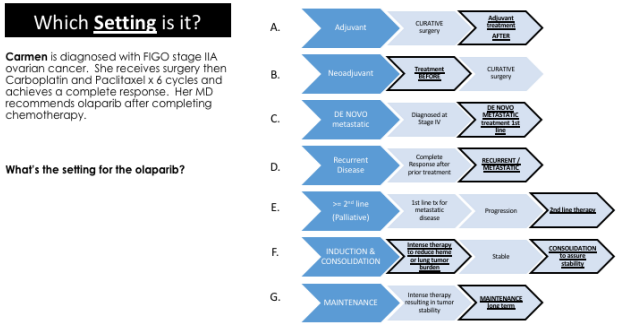
0:50:40

- Setting for Frank is de novo metastatic. He was diagnosed with liver metastases at the same time he was diagnosed with his primary colon cancer.
- Setting for George is recurrent metastatic. He had a period of complete response after chemo and surgery.
- This treatment considered first line in both of them.
- Even though George had prior therapy in the adjuvant setting, the setting would not be considered part of that line.



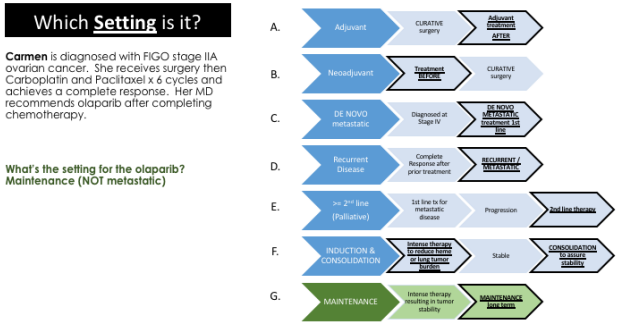
0:51:34

- Carmen is diagnosed with stage2a ovarian cancer. Gets surgery and carboplatin and paclitaxel and achieves complete response. MD recommends olaparib after chemo. What's the setting?



0:52:17

- Setting is maintenance, because she achieved complete response initially. MD assumed her cancer had high risk of recurrence.
- Not recurrent but maintenance because it was part of initial therapy package.



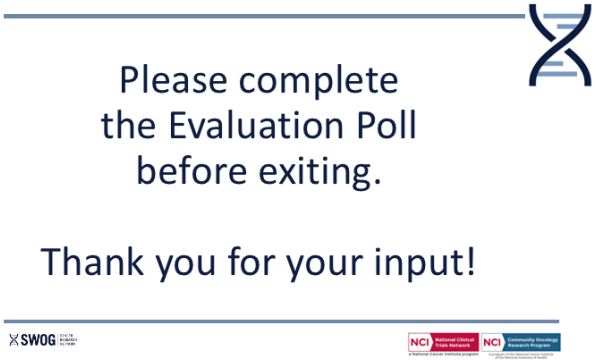
0:52:58
Abueg invited questions and suggestions via email.

0:53:45
Parker invited questions.

- No questions were asked

Conclusion and Evaluation Poll
0:54:36
Parker asked attendees to remember to complete the evaluation form (displayed below) prior to leaving the meeting.

Also noted slides and presentations would be posted to the SWOG website.



0:55:19
Meeting adjourned.

Open Forum Poll Questions for Session B:

• *Overall, the Lost to Follow-Up topic is applicable to my current work.*
1 = strongly agree 2 = somewhat agree 3 = somewhat disagree 4 = strongly disagree

• *The presenters were effective and knowledgeable about the topic.*
1 = strongly agree 2 = somewhat agree 3 = somewhat disagree 4 = strongly disagree

• *Overall, the Cancer Therapies topic is applicable to my current work.*
1 = strongly agree 2 = somewhat agree 3 = somewhat disagree 4 = strongly disagree

- *The presenter was effective and knowledgeable about the topic.*

1 = strongly agree 2 = somewhat agree 3 = somewhat disagree 4 = strongly disagree

- *What topics would you like to see at future Open Forums? (Open text field)*

- *Additional Comments: (Open text field)*