Scientific Impact of the CRA

Michael LeBlanc

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S1826 Phase III

Coordinating Group: SWOG

A Phase III, Randomized Study of Nivolumab (Opdivo) plus A Brentuximab Vedotin (Adcetris) plus AVD in Patients (Age >/= with Newly Diagnosed Advanced Stage Classical Hodgkin Lym

Date Activated: 07/19/2019

Date Closed: 12/01/2022

Participants: SWOG, CTSU (Supported by Alliance, CCTG, COG, ECOG-ACRIN)

Study Chairs: A Herrera, J Friedberg, S Castellino (COG), S Parsons (QOL)

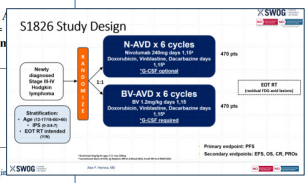
Study Champions: S Rutherford (Alliance), K Davison (CCTG), A Punnett (COG), A Evens (ECOG-ACRIN)

Data Coordinators: G Herbert, L Wells, A Rangel, D Chugu

Protocol Project Managers: C Miwa, K Gasic

Statisticians: M LeBlanc, H Li, J Unger (QOL), R Vaidya (QOL)

Example: Why is quality and timeliness critical ?



High accrual during early COVID

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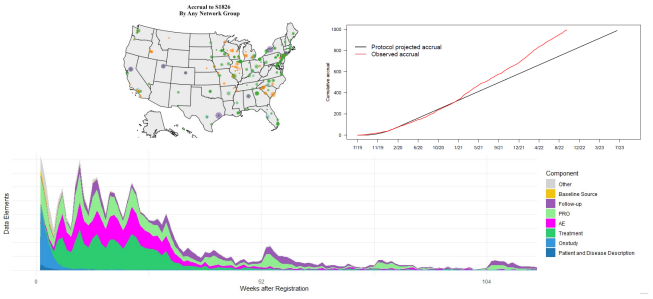
Data Flow



From the Rave logs of every data element entered

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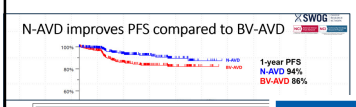
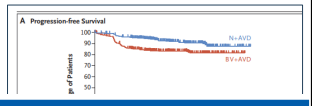
S1826: Data Quality and Monitoring Plans Matter





Nivolumab+AVD in Advanced-Stage Class

March 20, 2026

FDA APPROVAL ALERTS

FDA Approves Nivolumab with Chemotherapy for Previously Untreated Hodgkin Lymphoma

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Stages of Treatment Testing

- Phase I
  - The safe dose range, side effects, early activity.
- Phase II
  - Sufficient promise for further testing, more side effect assessment, refinement of dose, evidence of disease subtypes with most promise and feasibility.
  - Some design examples: single arm 2-stage, single arm pilot, multi-arm randomized (screening or selection).
- Phase III
  - Formal comparison of new treatment to standard treatment.

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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

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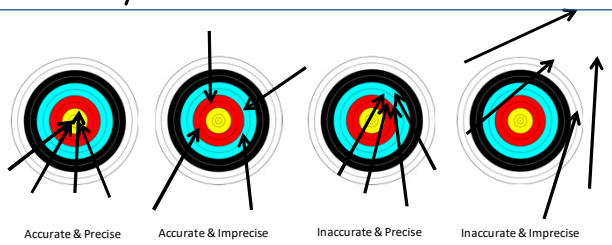
Variability and Bias



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How do we control variability?

- Eligibility criteria

  Example: Results of studies which allow only patients with local disease and performance status 0-1 will be less variable than those from studies allowing any stage and any performance status.

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How do we control variability? (cont.)

- Sample size

  Larger numbers of patients lead to reduced variability.

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The CRA's Role in Reducing Variability

- Verification of eligibility
- Avoidance of deviations from protocol treatment plans
- Submission of complete and timely data

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Bias

- 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.
- Example

  If a study of a treatment intended for patients with local disease includes a number of patients with more advanced disease, the treatment's efficacy may be underestimated.
- Solution

  Ensure adherence to eligibility criteria

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Bias

- Another Example

  If patients in an adjuvant therapy arm of a comparative study are followed more closely than those in an observation arm, the benefit of the adjuvant therapy may be underestimated.

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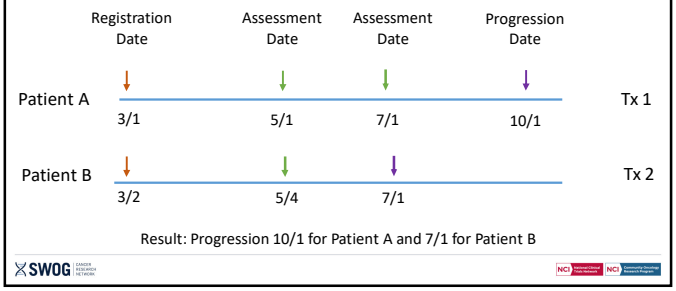
Illustration of Impact Lost to Follow-up



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

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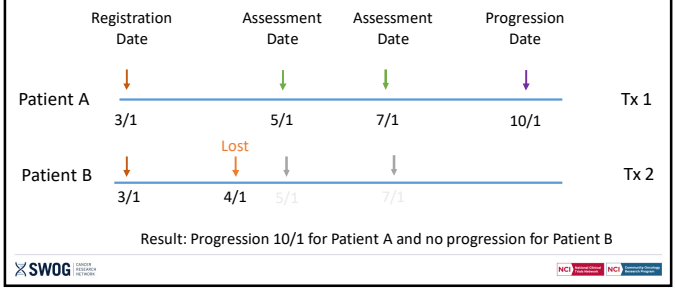
Illustration of Impact Lost to Follow-up



Result: Progression 10/1 for Patient A and no progression for Patient B

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Bias

- Solution
  - Ensure adherence to protocol requirements for follow-up examinations
- Schedule
  - Have patients return for evaluation according to protocol schedule
- Tests
  - Have all required tests performed at each evaluation

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The CRA's Role in Controlling Bias

- Verification of eligibility
- Adherence to protocol follow-up requirements

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Variability and Bias in Survival Data

- Survival - how long patients live after entering a study - is often the most important outcome we study
- Incomplete data increases both variability and potentially bias in studies of survival

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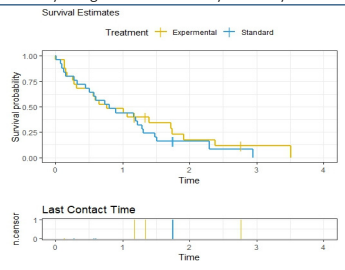
Estimated Survival

Study design: accrued over 3 years + 1 year of follow-up



Correct conclusion: new treatment does not help survival outcome

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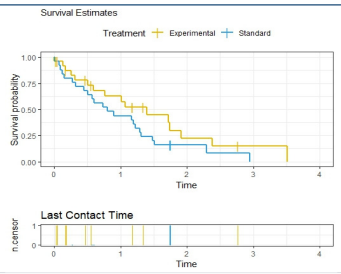
Estimated Survival

Some Patients lost to follow-up on one arm



Incorrect conclusion: new treatment helps survival outcome

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What We Need

- Complete and timely submission of accurate data including
  - Thorough documentation of all eligibility criteria
  - Complete description of all treatment received, whether according to protocol or not
  - Complete description of objective status and toxicities at every evaluation

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Effect of Non-dropout or Non-adherence on Sample Size

New sample size = sample size ÷ $(1\text{-}r)^2$

Non-adherence Rate	Sample Size (Example)
0%	100
10%	123
20%	156
30%	204
40%	278

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WHY IS IT ALWAYS CRITICAL?

Trial Monitoring

- Accrual monitoring (Stats, SC)
- Adverse event monitoring
  - SC, Stats, AE coordinator
  - CTEP-AERS reporting
  - Monthly reports (AE and dose summaries)
- Interim Analyses
- Data and Safety Monitoring Committee (DSMC)
- NEED HIGH QUALITY CURRENT DATA TO MAKE CRITICAL RECOMMENDATIONS

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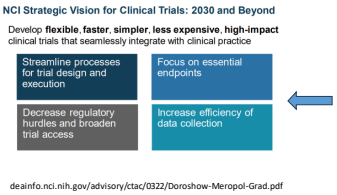
Next - Streamlining Clinical Trials



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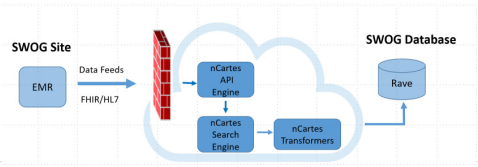
Alternative: Make it easier get data: SWOG-nCartes EMR-to-EDC Platform

- Decrease the burden of clinical trials reducing site data entry time and costs, increasing data quality, and reducing study queries
- Support for structured and unstructured data



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Time Savings/Reduce Errors

- Varies by study - highest value with structured (numeric) source data
- On the SWOG-nCartes studies rolled out, for most, the time savings is substantial
- SWOG sites estimate 50% or greater time savings on structured data with nCartes. Total time savings depends on form complexity and the amount of structured data
- Observed higher error rates reduced to approximately 0 in other specific structured data settings
- Some errors may be found in subsequent data review, reducing Rave queries, will substantially reduce effort at both sites and SDMC
- https://ncartes.com/videos/Sarah-Salter-1.html

Garza et al., Medical Informatics Europe Conference, 2024
Goodman et al. Journal of the Society for Clinical Data, 2025

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High quality and timely data are essential for good studies.

Your efforts are essential for high quality data.

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SWOG CANCER RESEARCH NETWORK

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