U01 MD Baseline In-Depth Interview Questions

You recently agreed to participate in a study that aims to explore the use of whole exome sequencing (WES) in the care of lung/colon cancer patients. WES is different from the current PROFILE study in a couple of ways. First, whereas PROFILE focuses on a defined set of alterations in a limited set of cancer-related genes, WES can detect alterations in the coding regions of any gene. Second, PROFILE currently only looks at the somatic, or tumor, genome. In contrast, for this study, we will be conducting WES of both the tumor and the germline genomes. In this interview, we will be asking about your expectations regarding sequencing of both tumor DNA and germline DNA.

All alterations will be reviewed by the newly formed Cancer Genomics Evaluation Committee at the Dana-Farber Cancer Institute and confirmed in a CLIA lab before they are returned to the treating oncologist.

I am going to ask you some questions today about your impressions and expectations related to the use of WES in your patients' care. I understand that we are asking you questions that might be difficult to answer. I also understand that it may be hard to anticipate what WES use will be like for you, as you have not routinely used WES in your clinical practice. However, it's very helpful for us to get a sense of what you anticipate might happen; in one year we'll talk again, and I'll ask what your actual experiences were like.

1) Anticipated benefits, risks and challenges of whole exome sequencing of tumor DNA:

Next, I would like to ask you what you anticipate will be the benefits, risk and challenges as whole exome sequencing of tumor DNA becomes incorporated into clinical practice.

- What do you anticipate will be the benefits **for your patients** as you incorporate whole exome sequencing **of tumor DNA** into their care?

- What do you anticipate will be the risks **for your patients** as you incorporate whole exome sequencing **of tumor DNA** into your practice?

    - Probes
        - Data volume
        - Inaccuracy/misinterpretations
        - Sequencing results for which there is no targeted therapy
        - Patients overwhelmed by too much information
        - Cost to patient
        - Repeated testing/biopsies
        - Delay treatment
        - Anything else?

- What do you anticipate will be the challenges **for you** as you incorporate whole exome sequencing **of tumor DNA** into your patients' care?

  - Probes:
    - Interpreting test results
    - Deciding what to disclose
    - Explaining test results
    - Addressing psychosocial concerns
    - Fitting discussions into oncology visits
    - Anything else?
    - What do you think will be the biggest challenge (for your patients or you?)? Why?

2) Intentions related to test result disclosure from tumor DNA

Whole exome sequencing of tumor DNA can yield a variety of different types of test results. For example, results may reveal predictive information- which can help inform treatment selection- as well as prognostic information.

Now I'm going to ask you about 4 different types of results from tumor DNA that you might anticipate disclosing or consider **not** disclosing to your patients.

- 1. Do you think you will disclose sequencing results that suggest a patient may benefit from a **targeted therapy that is FDA-approved for a *different* cancer**? Why/why not?

  - What factors will make you more likely to disclose a result? Less likely to disclose a result?

    - Probes (*reflect on answer*):
    - Anything about the patient?
    - Disease?
    - Potential treatment?

- 2. Do you think you will disclose sequencing results that suggest a patient may be eligible for a **clinical trial of a targeted therapy**? Why/why not?

  - What factors will make you more likely to disclose a result? Less likely to disclose a result?

    - Probes (*reflect on answer*):

- Anything about the patient?
- Disease?
- Potential treatment?

- 3. Do you think you will disclose sequencing results that have **positive prognostic implications** for your patient, but don't inform decisions about treatment? Why/why not?
    - What would influence your decision?

- 4. Do you think you will disclose sequencing results that have **negative prognostic implications** for your patient, but don't inform decisions about treatment? Why/why not?
    - What would influence your decision?

3) **Informed consent for whole-exome sequencing of tumor DNA**

- When thinking about the use of whole-exome sequencing of tumor DNA in your practice (in the future), do you anticipate having informed consent conversations with your patients before ordering sequencing of their tumor DNA?
    - Why/why not?
    - *If yes*: What are the main issues you expect to discuss during those informed consent conversations?

      Probes:

      What risks do you expect to discuss during the IC process?

      What benefits do you expect to discuss during the IC process?
    - *If no*: Are there any risks of whole-exome sequencing of tumor DNA that you think patients should consider before sequencing is performed?

4) Anticipated benefits, risks and challenges of whole exome sequencing of germline DNA:

As I noted previously, performing whole-exome sequencing of tumor DNA requires that whole-exome sequencing of germline DNA be performed in parallel. This sequencing of germline DNA may lead to findings of relevance to your patients. Next, I would like to ask you what you anticipate will be the benefits, risk and challenges as whole exome sequencing of **germline DNA** becomes incorporated into clinical practice.

- What do you anticipate will be the main benefits **for your patients** as you incorporate whole exome sequencing **of germline DNA** into your practice?

- What do you anticipate will be the main risks **for your patients** as you incorporate whole exome sequencing **of germline DNA** into your practice?
    - Probes (concerns that have been found in prior research)
        - Data volume
        - Uncertain nature of results
        - Unanticipated/unintended findings
        - Family member implications
        - Emotional risk of patients learning information that they might not be ready to hear.
        - Unnecessary info for the patient to have
        - Potential for discrimination (e.g., health insurance) due to genetic predispositions
        - What do you anticipate will be the main challenges **for you** as you incorporate whole exome sequencing **of germline DNA** into your practice?
    - Probes:
        - Interpreting test results
        - Deciding what to disclose
        - Explaining test results
        - Patient and family member responses to the test results.
        - What do you think will be the biggest challenge (for your patients or you)? Why?

5) Intentions related to test result disclosure

Whole exome sequencing of **germline DNA** can yield a variety of different types of test results. For example, results can reveal information about cancer risk, risk of non-cancer disease, and pharmacogenetic information.

Now I'm going to ask you about 5 different types of results from **germline DNA** that you might anticipate disclosing or consider **not** disclosing to your patients.

- 1. Do you think you will disclose germline results suggesting that your patient has an inherited predisposition to *cancer*? Why/why not?
    - What would influence your decision?

- 2. Do you think you will disclose germline results suggesting that your patient has an inherited predisposition to *a disease other than cancer*? Why/why not?

- What would influence your decision?

- 3. Do you think you will disclose pharmacogenetic results that might influence your use of cancer drugs? Why/why not?

    - What would influence your decision?

4. Do you think you will disclose pharmacogenetic results that might influence your use of noncancer drugs? Why/why not?

    - What would influence your decision?

- 5. Do you think you will disclose germline results suggesting that your patient is a carrier of an autosomal recessive mutation that is associated with serious manifestations in individuals who inherit two copies of the abnormal gene? Why/why not?

    - What would influence your decision?

6) **Informed consent for whole-exome sequencing of germline DNA**

- When thinking about the use of whole-exome sequencing of tumor DNA in your practice, do you anticipate having informed consent conversations with your patients before ordering sequencing of their germline DNA?

    - Why/why not?

    - *If yes:* What are the main issues you expect to discuss during those informed consent conversations?

        - *If no risks mentioned*: Any risks?
        - *If no benefits mentioned*: Any benefits?

    - *If no*: Are there any risks of whole-exome sequencing of germline DNA that you think patients should consider before sequencing is performed?

6) Closing

Is there anything else that you would like to say about using whole exome sequencing in your practice?

What types of resources would be helpful to you, in integrating WES into your practice?

Thank you very much for participating in this interview. We greatly appreciate all of your time and effort.

If you have any questions or concerns, please contact Drs. Steven Joffe or Stacy Gray.