3.88 Behind the Scenes for the One-Year Anniversary of Malignant with Dr. Vinay Prasad

↗ Type	Plenary Session

We Discuss:

Introduction [1:06]

- **YouTube**
  - Watch this conversation on YouTube

Malignant

- Malignant: How Bad Policy and Bad Evidence Harm People with Cancer

Question 1 [1:57]

Where were you in your career? Where did the idea for this book originate?

> "My working habits are simple: long periods of thinking, short periods of writing." - Hemingway

> "I didn't have time to write you a short letter, so I wrote you a long one." - Twain

Question 2 [6:24]

What was one of the most surprising things you learned while writing Malignant?

- When is crossover desirable in cancer drug trials and when is it problematic?
    - Haslam & Prasad, Annals of Oncology

Table 1. An explanation of how crossover can occur or not occur, be desirable or problematic, or any combination of these two

	Crossover occurred	Crossover did not occur	Uncertainty as to whether crossover occurred
Crossover is desirable: Situations in which the experimental drug has ALREADY proven benefit in a later line of therapy or is standard of care in the latter line	KEYNOTE-024 trial [6] tested whether platinum doublet or PD-1 antibody was superior in the front line of NSCLC. As PD-1 antibody therapy had already been approved in the second line, the trial is essentially testing whether upfront administration is superior to current standard of care (as second line). In fact, crossover was permitted and 43.7% of control arm crossed over to pembrolizumab.	In the LATITUDE trial [7], 1199 patients with castrate sensitive metastatic prostate cancer were randomized to receive androgen-deprivation therapy, with or without abiraterone. Before this trial, standard of care was to administer abiraterone to these patients in a later line of therapy. As such, Prasad and Berger wrote 'we cannot be sure that the survival advantage of early treatment would still exist if control patients had fair access to this drug' [13].	The PACIFIC trial [9] tested whether, for patients with stage III lung cancer, 12 months of Durvalumab improved PFS and OS. For patients whose disease recurs however, the trial does not specify whether and to what degree they receive PD-1 therapy. Given the trial was conducted at many global sites, one concern is control arm patients may not receive these drugs as they would in the USA. This would not affect the PFS estimate, but may affect OS.
	DESIRABLE SITUATION	**UNDESIRABLE SITUATION**	**UNDESIRABLE SITUATION**
Crossover is problematic: Situations in which the fundamental efficacy of the experimental agent has not been established in any prior study	In the randomized trial leading to regulatory approval of sipuleucel-T [9], 225 patients were randomized to the vaccine or placebo. Patients who progressed were allowed to receive a similar drug as sipuleucel-T (a frozen salvage product). Disease progression and PFS were not improved, yet overall survival was. This led to the suggestion in an AHRQ report that sipuleucel-T exhibited efficacy not by improving outcomes but rather because crossover harmed the control group by delaying alternate effective therapy. In this case, fewer patients received docetaxel in the control arm and, on average, after a delay.	In the CLEOPATRA study [11], patients with HER2-positive metastatic breast cancer were randomly assigned to receive trastuzumab and docetaxel, with or without the addition of pertuzumab. Crossover was not permitted before analysis of overall survival.	Occasionally, published trials do not clearly specify if crossover did or did not occur [14].
	UNDESIRABLE SITUATION	**DESIRABLE SITUATION**	**UNDESIRABLE SITUATION**

Question 3 [10:38]

Why do you think Malignant is a "must-read" for medical trainees or anyone interested in cancer evidence and health policy?

Question from the Audience [15:04]

Logan prefaces the question with a short story:

Logan tells a friend that in the oncology space, we are approving drugs based on outcomes that have little to do with the patient, but the problem compounds when one accounts that the price of these drugs has a large impact on society's tax dollars

His response and question is:

Where does this problem even start? What is the root issue?

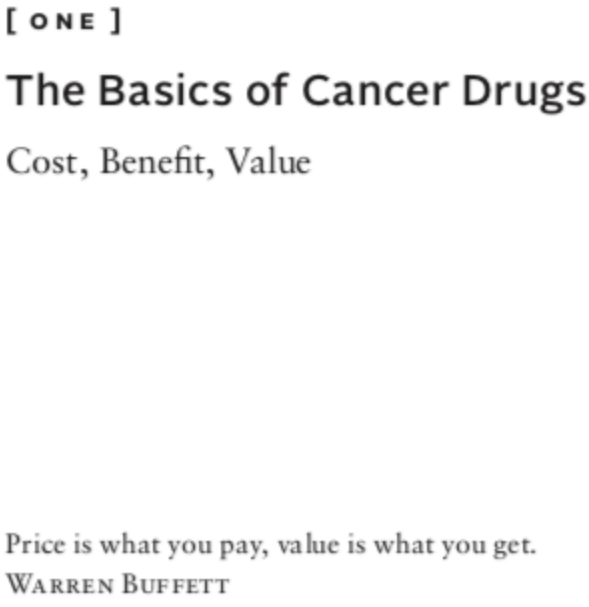
Question 4 [20:56]

Recently Dr. Prasad interviewed Dr. Avi Loeb, former department chair of astronomy at Harvard. He has two common phrases he likes to use:

1) Follow the evidence 2) Keep your eye on the ball

In the context of Malignant, where we are or are we not following the evidence? Are we keeping our eye on the ball?

Question 5 [28:36]



What is this concept of value in the oncology space?

Question 6 [31:40]

A reporter once told Dr. Prasad:

> *"Be careful of medical treatments where every news outlet covers the SAME patient. If you can only find one person that did well, that might not be such a great therapy"*

How much of a role do you think anecdotes play on the narrative around certain drugs? In the clinic, do patients present these anecdotes to you, and how do you respond to them?

Question 7 [41:23]

Dr. Peter Attia talks about the 4 A's of being a physician:

1) Affable

2) Available

3) Advocating

4) Ability (competence)

Malignant touches upon the theme of "ability" a lot, such as navigating the decision tree, would you expand upon what it means to be an able oncologist?

Question 8 [47:23]

Is interpreting cancer evidence difficult? Why is there so much dispute around so many trials? Shouldn't the evidence be clear?

Question 8 [54:55]

Recently Dr. Prasad has shown interest in the Surgeon General's recent conflicts of interest

- Op-Ed: Vivek Murthy's Multimillion Dollar Conflicts Are Cause for Concern
    - Prasad, MedPageToday

I would like you to touch upon the impact of the industry's influence from a macro perspective but also a micro. **How does it affect the system? How does it affect the physician prescribing the medication?**

Questions from Dr. Christopher Booth of Queen's University in Kingston, Ontario [1:01:24]

“What (if anything) would you have done differently in your training and in your first 5 years of faculty?” - Dr. Booth

Question 9 [1:09:49]

Similar to Nassim Taleb's *Incerto*

Will there be a 3rd book in this installment? If so, will it be oncology related?

Question 10 [1:11:59]

This is a question adopted from Tim Ferriss, but modified for the context of this discussion

“What advice would you give to a smart, driven medical trainee about to enter the “real world of oncology”? What advice should they ignore?”

People mentioned

- Sham Mailankody, MBBS
- Sidney Farber

Literature mentioned

- BELLINI
  - Kumar et al., The Lancet
- Should I Be Tested for Cancer? : Maybe Not and Here's Why
  - Gil Welch
- Less Medicine, More Health: 7 Assumptions That Drive Too Much Medical Care

    - Gil Welch
- Overdiagnosed: Making People Sick in Pursuit of Health
    - Gil Welch
- The Death of Cancer: After Fifty Years on the Front Lines of Medicine, a Pioneering Oncologist Reveals Why the War on Cancer Is Winnable--and How We Can Get There
    - DeVita
- Emperor of All Maladies: A Biography of Cancer
    - Mukhurgee
- The Laws of Medicine: Field Notes from an Uncertain Science
    - Mukhurgee
- House of God
    - Samuel Shem

Plenary Session is a podcast on medicine, oncology, & health policy.

Host: Vinay Prasad, MD MPH from University of California, San Francisco.

Tweet your feedback to @Plenary_Session or e-mail plenarysessionpodcast@gmail.com.

Written By: Kerrington L. Powell B.S.