

1 DR. DUTCHER: Other comments?

2 DR. NETTO: May I?

3 DR. DUTCHER: Sure.

4 DR. NETTO: Just a general comment, starting
5 with the tissue issue.

6 I think this is the time for us to really
7 bite, because it's KRAS and second to HER2, and like it
8 was said that oncology seems to be leading the way in
9 predictive markers. I think this is very timely to
10 think about how future studies should be designed up
11 front and how standardization should be thought of at
12 that time of discovering the biomarker or thinking of
13 the hypothesis, because this will be emulated and I
14 think it will make our lives all easier down the road
15 when we're faced with other trials. So I think it's a
16 very important thing.

17 DR. DUTCHER: Dr. O'Neill?

18 DR. O'NEILL: I would sort of second that.
19 We haven't had much discussion about what would be the
20 design of a study if we wanted to do it in the future.
21 There was a lot of emphasis on the retrospective design
22 and how could we do that to the quality of where it

1 might be acceptable.

2 But there's a fair amount of literature going
3 on, and some people here know about this, under
4 adaptive designs, prospective adaptive designs. And
5 there's the opportunity for this to be done right in
6 terms of at least evaluating all comers and then making
7 some decisions about whether it's worth continuing in
8 certain subgroups and then going forward and enriching
9 the trial with more of, let's say, mutant, a wild type,
10 or whatever. And I think those are not huge trials. I
11 think the research shows that they can be relatively
12 efficient.

13 So I think that it would be nice to have a
14 discussion like that about, okay, this is inning one of
15 this game and this is what we did, but where are we
16 going to go so we don't have to revisit these kinds of
17 discussions too much in the future. I think there was
18 a certain feeling that, well, we're stuck with this and
19 this is the way it's going to be. I'm not so sure it
20 needs to be that way.

21 I think that there has also been an undertone
22 of prospective planning and get it right and how does

1 the sequence of studies fit together. This is all
2 under that adaptive design thinking, not exploratory
3 adaptation, but pre-specification for adaptation in a
4 measured way where we would learn many things, some of
5 which may solve CDRH's issues, also.

6 DR. DUTCHER: Thank you. I think it's
7 important that we all -- all of us here have lived
8 through the moving target of things that were
9 predictive or prognostic, and things change, and
10 certainly this may change. And the point that there
11 are other downstream genes or proteins that may be
12 mutated is a very important point.

13 So I think this is really just the beginning
14 of trying to figure out what goes into those patients
15 who don't respond.

16 Other comments from the group?

17 DR. PAZDUR: Thank you very much.

18 DR. DUTCHER: All right. So this meeting is
19 now adjourned. Thank you all.

20 (Whereupon, at 3:28 p.m., the meeting was
21 adjourned.)

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