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Examining Patient Choices for Metastatic Breast Cancer Drugs: Using Conjoint Analysis to Examine Attributes of Paclitaxel and Capecitabine

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Background:
Patients with metastatic breast cancer face difficult drug decisions. Our previous research (ASCO Proc 2011, abstr 6044) focused on general benefit and toxicity showed that conjoint analysis (CA) allows patients to express preferences; our current research quantifies patient preference for specific drug profiles (capecitabine and paclitaxel).

Methods:
Research Advocacy Network and CBWhite conducted research using CA for DOD Center of Excellence for Individualization of Therapy in Breast Cancer. An online survey was sent by four breast cancer organizations (N=641). Questions elicited views on trade-offs between benefit and type/severity/duration of toxicity. CA questions present pairs of hypothetical treatments and ask respondents their preferred alternative; a follow-up question asks whether the person would take the treatment if it were the only option available. Analysis of response patterns allows study of treatment preferences for combinations of benefit and described toxicity.

Results:
See table. Preferences show much greater attention to benefit than to toxicity. When CA is used to examine impact of biomarkers, focus on benefit continues. Paclitaxel profile (IV) set with moderate PN lasting 1 year post treatment: with 33% benefit LH, 6% of respondents change treatment decision if biomarker predicts 27% vs 60% toxicity LH; with 27% toxicity LH, 22% of respondents change treatment decision if biomarker predicts 20% vs 50% benefit LH.

Prediction of % Selecting Treatment with Benefit and Toxicity Likelihood (LH) Under Two Scenarios (N=641)

Benefit LH	Toxicity LH 10%	20%	40%	60%
IV drug profile- moderate peripheral neuropathy (PN) for 1 year				
20%	N/A	77.4	72.3	65.3
30%	N/A	89.8	86.4	81.6
50%	N/A	97.1	96.1	94.3
Oral drug profile- moderate Hand-Foot Syndrome during treatment				
10%	67.6	65.2	60.8	N/A
30%	94.7	93.0	91.4	N/A
50%	99.0	98.3	97.4	N/A

Conclusion:
For patients with metastatic disease, CA shows much greater attention to benefit than toxicity, and high likelihood to take treatment with at least 30% chance of benefit for any toxicity tested here. These results suggest biomarkers (for the profiled drugs) predicting benefit are more likely to be used to affect patient treatment decisions than biomarkers for toxicity.

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KEY QUESTIONS/AIMS OF THE PROJECT

Using two drug profiles, measure patient preferences to learn:

- How may information from specific biomarkers influence patient decision making?
- How do patients weigh the risks and benefits of specific treatment attributes during decision making?

PROCESS

- 2010 pilot study (focus groups, survey, data collection, analysis, and report) based on general attributes describing benefit and side effect
- Selection of specific drug profiles for investigation (paclitaxel and capecitabine)
- Survey development; Pretest; Survey revision and re-test
- Data collection (Metastatic Breast Cancer Network -307 responses; Living Beyond Breast Cancer -213 responses; Young Survival Coalition -75 responses; BCMets listserv -46 responses)
- Data analysis and report

RESPONDENT PROFILE HIGHLIGHTS

- The respondents have high levels of education and income; most are Caucasian.
- Over 1/4 diagnosed over ten years ago.
- For almost 1/4, metastasis was discovered at initial diagnosis. About 3/4 have been living with metastasis for less than five years.
- Two-thirds have no family history or known mutation.
- Over 70% indicate they are in treatment, with disease evident and stable/responding.
- Almost half live within a half-hour of their treatment site.
- Self-reported quality of life (QOL) is high.

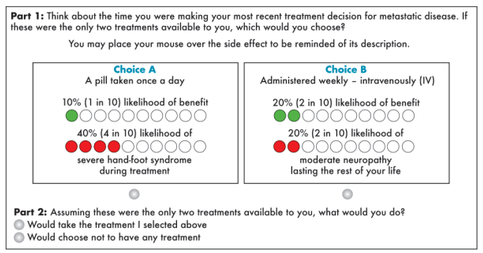
CONJOINT ANALYSIS

Conjoint analysis is a specialized market research technique often used to better understand the needs or values of respondents. In this case, we used paclitaxel and capecitabine profiles to select variables to be tested, to gather patient preferences that would link to actual treatments.

Respondents were not asked whether they would choose either drug by name; they saw hypothetical treatments using variables that can describe the two drugs:

- Method of administration
- Likelihood of benefit (defined as shrinkage of advanced cancer)
- Likelihood of side effect, description of side effect type, severity, and duration

Respondents saw 14 questions, each with two hypothetical treatments, described as the only drugs available, and were asked: (1) which they would choose and (2) whether or not they would take the treatment.



Note: In pretest, two-part question helped respondents carefully consider the option not to treat. Lengthy descriptions of each side effect were provided and accessible during the conjoint questions.

For the objectives of this analysis, we have used the conjoint model to:

- Examine the trade-offs in the situation in which only one treatment is available (what percent of respondents are predicted to take the treatment versus not).
- Attempt to mimic the biomarker choices to see what conjoint analysis predicts the impact of the various spreads and types of information to be.

As with any model and any market research, the predictions are not meant to suggest we know how many people will take particular actions. In this case, many variables are not accounted for, such as the role and advice of the medical team, the opinions of family members and friends, other options that may exist, and the comprehension/ understanding of the choices. In addition, a survey question about hypothetical choices is different than the reality of disease and treatment. That said, the conjoint questions have provided a format for patients to express trade-offs and preferences. By examining the predicted choices in a relative sense, we gain an understanding of what patients think they might do and what seems to be more and less important to them.

SURVEY FINDINGS

Basic Tradeoffs

The charts below show the predicted likelihood of choosing a treatment with the characteristics specified. In each case, several variables are held constant (noted as "FIXED") to examine the pairwise tradeoffs.

As expected, likelihoods of taking treatment are higher for higher benefit or lower toxicity. It is also notable that:

- In the ranges tested, respondents are more sensitive to benefit than to toxicity.
  - Much steeper declines in likelihood of taking treatment as benefit decreases than as toxicity increases (Charts 1 and 2)
  - Relatively high likelihood of taking treatment for any description of toxicity at the fixed levels of benefit tested (Charts 3 and 4).
- There are apparent thresholds.
  - At 10% likelihood of benefit, far fewer respondents appear likely to take treatment, with likelihoods of taking treatment hovering at or below 50% (Chart 2).
  - For the most part, toxicity needs to reach 60% to see much drop-off in likelihood to take treatment (Charts 1 and 3).
- Within toxicity, severity, duration, and type of side effect patterns emerge.
  - With peripheral neuropathy (PN), increasing severity from moderate to severe OR duration from "during treatment" to one year past treatment seem to cause similar drops in likelihood of taking treatment. (Chart 3).
  - Diarrhea and Hand-Foot Syndrome (HFS) seem about equal in respondents' minds, at least when considering moderate and severe levels of each. The change from moderate to severe levels of either side effect caused reductions (quite similar to the reductions seen with PN) in likelihood to take treatment (Charts 3 and 4).

In the charts, we have included solid lines between levels that are continuous in some way and dotted lines between levels that are discrete.

Benefit versus Toxicity Likelihood
CHART 1

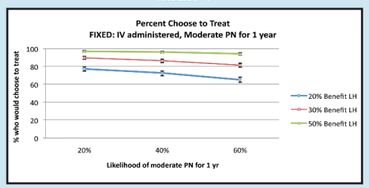
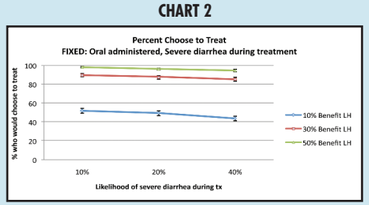


CHART 2



Toxicity Likelihood versus Toxicity Description
CHART 3

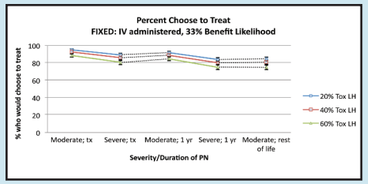
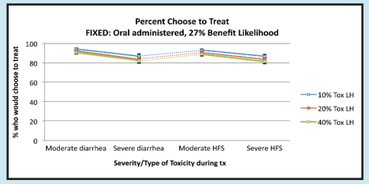


CHART 4



Subgroup Analysis

The data above has been examined amongst many different subgroups of respondents. Some top findings:

- Age of respondent: Respondents under age 50 exhibit higher likelihoods to take treatment and those over age 50 have lower likelihoods.
- Presence and age of children: Those with children under age 18 have higher likelihoods to take treatment and those with children under age 12 have even higher likelihoods in most model runs. Those with adult children and those with no children have lower likelihoods.
- Proximity to treatment site: An interesting result relates to proximity to treatment site, with those needing to travel less than a half hour showing significantly higher likelihoods to take treatment.
- Chemo experience: Those who have taken capecitabine exhibit higher likelihoods to take a drug with a capecitabine profile; those who have taken a taxane exhibit higher likelihoods to take a drug with a paclitaxel profile.
- Experience with HFS: Those who have had HFS have consistently higher likelihoods to take treatment. This particular side effect shows this pattern more consistently and strongly than any other side effect.

Modeling Biomarkers

Even though the conjoint exercise itself did not make reference to biomarkers, we can run the model at the levels of benefit and toxicity suggested by biomarkers to see if respondents indicate different preferences. For instance, if a biomarker will tell people they are either 30% or 50% likely to benefit from a treatment, we can see what the model predicts regarding selecting treatment at each of those levels; this provides a measure of the potential influence of biomarker information.

In this case, we based our model runs on particular descriptions of possible biomarkers for each drug's profile. Here are the scenarios tested, with column labels indicating which drug profile was used and which type of biomarker was modeled:

	Paclitaxel Toxicity Biomarker	Paclitaxel Benefit Biomarker	Capecitabine Toxicity Biomarker	Capecitabine Benefit Biomarker
Administration	IV	IV	Oral	Oral
Benefit (fixed or biomarker range)	33% fixed	20% versus 50% biomarker	27% fixed	13% versus 40% biomarker
Toxicity (fixed or biomarker range)	27% versus 60% biomarker	27% fixed	10% versus 40% biomarker	10% fixed
Toxicity type/ severity/duration	moderate PN 1 year	moderate PN 1 year	severe diarrhea	severe diarrhea

In Table 1 below, we show results based on examining the percent of respondents who are predicted by the model to:

- Take treatment at either "end" of the biomarker
- Not take treatment at either "end" of the biomarker
- Take treatment at the "good end" of the biomarker and not take treatment at the "bad end" of the biomarker (labeled as "switch")

These results indicate that:

- Benefit biomarkers in the ranges tested are predicted to have far greater influence than toxicity biomarkers.
- The capecitabine benefit biomarker is likely to show the highest degree of switching impact due to the range covered (13% to 40% benefit) as it spans important thresholds.

TABLE 1

	Paclitaxel Toxicity Biomarker	Paclitaxel Benefit Biomarker	Capecitabine Toxicity Biomarker	Capecitabine Benefit Biomarker
Take treatment	84.7	75.7	82.1	61.8
Do not take treatment	9.1	3.2	12.8	4.1
Switch	6.2	21.1	5.1	34.1

To further examine the possible influence of biomarker information, we tested these same biomarkers in the model with both drug profiles available: capecitabine and paclitaxel. We sought to predict whether the biomarker might influence drug selection, not just whether or not to take treatment. These results are more complicated because more possibilities exist.

The results are outlined below (Table 2), with the rectangles surrounding the numbers influenced by the biomarker. We see that:

- Benefit biomarkers continue to show very significant likelihood of influence.
- Toxicity biomarkers, while still less influential than benefit biomarkers, matter more in the selection of treatment than in the "no treatment" decision.

TABLE 2

	Paclitaxel Toxicity Biomarker (27% to 60% toxicity)	Paclitaxel Benefit Biomarker (50% to 20% benefit)	Capecitabine Toxicity Biomarker (10% to 40% toxicity)	Capecitabine Benefit Biomarker (40% to 13% benefit)
Paclitaxel-profile in either case	48.3	15.0	63.6	15.2
Capecitabine-profile in either case	30.3	7.3	17.9	5.8
"No treatment" in either case	6.0	2.4	6.0	2.9
Switch from paclitaxel-profile to capecitabine-profile	13.1	67.2	NA	NA
Switch from paclitaxel-profile to "no treatment"	2.2	8.1	NA	NA
Switch from capecitabine-profile to paclitaxel-profile	NA	NA	11.1	70.7
Switch from capecitabine-profile to "no treatment"	NA	NA	1.4	5.5

Somewhat limited subgroup findings with respect to biomarkers, given the high interest in the description of those who will switch, leaves us with ideas for future research. Perhaps adding a battery of attitudinal questions would better identify those who are predisposed to treat, those who want to avoid all or particular side effects, and the impact of having had a side effect. Such findings might allow oncologists to ask a limited set of questions that are most likely to identify particular patient attitudes toward treatment choices.

CONCLUSIONS

Key findings include the following:

- Within the ranges tested, benefit greatly outweighs toxicity in predicted decision-making.
- Severity of side effect seemed to have a greater impact on respondents than type of side effect, amongst the ranges and types we tested (moderate to severe PN, HFS, and diarrhea).
- Subgroup differences that seem interesting and informative:
  - Younger respondents and/or those with children under 18 seem more likely to take treatment, while respondents age 50 and over and/or those without children seem less likely to take treatment.
  - Those who live closer to their treatment site show higher likelihoods to take treatment.
- Biomarkers for benefit seem far more likely to influence treatment decisions than biomarkers for toxicity. Biomarkers may also be used differently depending on the situation. That is, if only one treatment is available, we see some predicted usage of biomarkers to decide whether to treat but, if two treatments are available, we see increased predicted usage as the biomarker can also be used to determine which treatment to take.

FUTURE DIRECTIONS

- Conduct this research with a more representative population (women of color, and women with lower income and/or educational levels).
- Continue to explore the patterns related to proximity to treatment site and to attitudes toward treatment.
- Examine preferences in the adjuvant setting.
- Examine preferences driven by other drug profiles to explore a wider range of side effects and, possibly, different types of benefit.

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