Ongoing trials are prospectively evaluating the ability of HRD score to predict response to cisplatin neoadjuvant chemotherapy in patients with Triple Negative Breast Cancer.

Andrea L. Richardson1,2,6, David D. Silver 1,6,*, Zoltan Szallasi3,6,7,*, Erica L. Mayer1,6, Nicolai J. Birkbak7,*, Zhigang C. Wang1,6,*, J. Dirk Iglehart1,2,6, Eric P. Winer1,6, Nadine M. Tung4,6, Paula D. Ryan, Steven J. Isakoff6,6,*, William T. Barry6,6,4, April Greene-Colozzi1, Alexander Gutin3,4, Julia Gull1,4, Chris Neff6, William T. Barry1,6,4, April Greene-Colozzi1, Alexander Gutin3,4, Julia Gull1,4, Chris Neff6, and Judy E. Garber1,6

### METHODS

**HRD Score** was defined as HRD < 42 (5th percentile of HRD scores in the tumors with BRCA1/2 mutation or mutational status). The distribution of the HRD score in the breast cancers is shown in Figure 1. HR-deficiency is defined as HRD score 42 or BRCA1/2 mutant.

**Archival formalin-fixed paraffin embedded core biopsy tumor samples** were obtained from 70 patients with TNBC from 2 neoadjuvant clinical trials conducted at DHFCC 1,2. Five to ten 5-micron tissue sections were sent to Myriad Genetic Laboratories. Eight samples had insufficient tumor tissue and were not processed. DNA was extracted from 62 samples and was analyzed using the HRD and BRCA1/2 sequencing assay. The distribution of HRD scores observed in this cohort is shown in Figure 2.

Pathologic response was categorized by the residual cancer burden (RCB) class9 with pathologic partial response (pPR) defined as RCB 0 or I and pathologic complete response (pCR) as RCB 0.

Pathologic response was also sensitive to platinum2,3. Further, several recent multicenter trials have shown improvement in overall survival in patients with breast cancer with homologous recombination deficiency (HRD) and have increased the use of platinum-based chemotherapy in this population1.

Primary analysis: HR deficiency status and response (n=50).

Secondary analyses: Quantitative HRD score and response (n=48).

### RESULTS

#### Multivariate model of pNP=50:

**Table 1** shows the results of the multivariate analysis for predicting cisplatin response. The HRD score (with the predefined threshold) was significant at predicting cisplatin response whereas neither BRCA1 mutation nor clinical variables were significant predictors.

**Ongoing trials** are prospectively evaluating the ability of HRD score to predict response to platinum-based chemotherapy in patients with triple negative breast cancer (NCT01982448).

### REFERENCES

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Title</th>
<th>Journal(s)</th>
<th>Year</th>
</tr>
</thead>
</table>

**Figure 1** illustrates the distribution of HRD scores observed in the cohort of 62 patients with adequate FFPE tumor tissue.

**Figure 2** shows the HRD score distributions for patients with BRCA1/2 mutated compared to non-mutated tumors (63.1 vs. 45.3; p-value = 0.015).

**Figure 3** demonstrates that HRD score = LOH + TAI + LST was used to test models of pPR, while Firth’s penalized likelihood was used to test pCR. All clinical and pathologic variables were included in the model, and the odds ratio was calculated using the HRD score as a continuous variable.

**Figure 4** shows the results of logistic regression analysis for predicting pPR and pCR. The odds ratio for pPR was 2.47 (95% CI: 1.91, 3.15), and the odds ratio for pCR was 2.29 (95% CI: 1.46, 3.62).

**Figure 5** illustrates the results of the multivariate analysis for predicting cisplatin response. The HRD score (with the predefined threshold) was significant at predicting cisplatin response whereas neither BRCA1 mutation nor clinical variables were significant predictors.

**Figure 6** shows the results of the multivariate analysis for predicting cisplatin response. The HRD score (with the predefined threshold) was significant at predicting cisplatin response whereas neither BRCA1 mutation nor clinical variables were significant predictors.

**Figure 7** demonstrates that HRD score = LOH + TAI + LST was used to test models of pPR, while Firth’s penalized likelihood was used to test pCR. All clinical and pathologic variables were included in the model, and the odds ratio was calculated using the HRD score as a continuous variable.

**Figure 8** shows the results of logistic regression analysis for predicting pPR and pCR. The odds ratio for pPR was 2.47 (95% CI: 1.91, 3.15), and the odds ratio for pCR was 2.29 (95% CI: 1.46, 3.62).

**Figure 9** illustrates the distribution of HRD scores observed in the cohort of 62 patients with adequate FFPE tumor tissue.

**Figure 10** shows the HRD score distributions for patients with BRCA1/2 mutated compared to non-mutated tumors (63.1 vs. 45.3; p-value = 0.015).

**Figure 11** demonstrates that HRD score = LOH + TAI + LST was used to test models of pPR, while Firth’s penalized likelihood was used to test pCR. All clinical and pathologic variables were included in the model, and the odds ratio was calculated using the HRD score as a continuous variable.

**Figure 12** shows the results of logistic regression analysis for predicting pPR and pCR. The odds ratio for pPR was 2.47 (95% CI: 1.91, 3.15), and the odds ratio for pCR was 2.29 (95% CI: 1.46, 3.62).

**Figure 13** illustrates the distribution of HRD scores observed in the cohort of 62 patients with adequate FFPE tumor tissue.

**Figure 14** shows the HRD score distributions for patients with BRCA1/2 mutated compared to non-mutated tumors (63.1 vs. 45.3; p-value = 0.015).

**Figure 15** demonstrates that HRD score = LOH + TAI + LST was used to test models of pPR, while Firth’s penalized likelihood was used to test pCR. All clinical and pathologic variables were included in the model, and the odds ratio was calculated using the HRD score as a continuous variable.

**Figure 16** shows the results of logistic regression analysis for predicting pPR and pCR. The odds ratio for pPR was 2.47 (95% CI: 1.91, 3.15), and the odds ratio for pCR was 2.29 (95% CI: 1.46, 3.62).

**Figure 17** illustrates the distribution of HRD scores observed in the cohort of 62 patients with adequate FFPE tumor tissue.

**Figure 18** shows the HRD score distributions for patients with BRCA1/2 mutated compared to non-mutated tumors (63.1 vs. 45.3; p-value = 0.015).

**Figure 19** demonstrates that HRD score = LOH + TAI + LST was used to test models of pPR, while Firth’s penalized likelihood was used to test pCR. All clinical and pathologic variables were included in the model, and the odds ratio was calculated using the HRD score as a continuous variable.