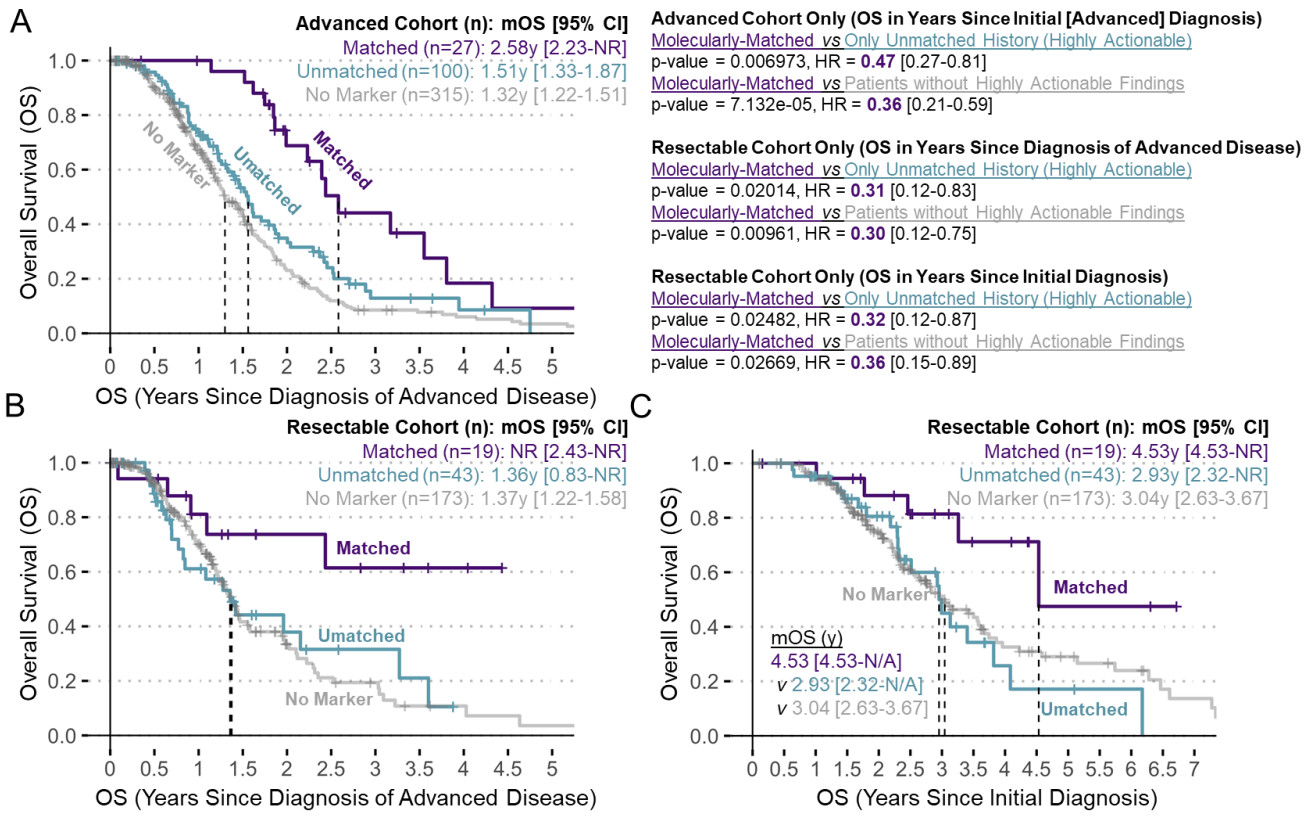
Actionable Molecular Findings	Implicated Class of Therapy	# Pts
Microsatellite Instability	Immunotherapy	10
HR-DDR Deficiencies	PARP inhibitors	152
ALK/ROS1/NTRK Oncogenic Fusions	ALK/ROS1/TRK inhibitors	5
FGFR/RET Activating Alterations	mult-targeted TKIs	8
EGFR Activating Mutations	EGFR inhibitors	2
HER2 Amplification/Overexpression	HER2 antibody combinations	8
BRAF Oncogenic Mutations/Fusions	BRAF/MEK/ERK inhibitors	21
PI3K/AKT/mTOR Pathway Alterations	PI3K/AKT/mTOR inhibitors	60
CDK4/6 Amplifications	CDK4/6 inhibitors	22
IDH1/2, NOTCH	Other targeted agents	8

Supplementary Table 1: Pathway-Level Summary of Actionable Findings. Examples of actionable findings and molecularly-matched therapeutic strategies across various biological pathways as assessed by Perthera's Molecular Tumor Board. Of note, the total number of actionable findings identified (296) is higher than the total number of patients with actionable findings (282/1082) because in some cases, a molecular report identified more than one actionable alteration.



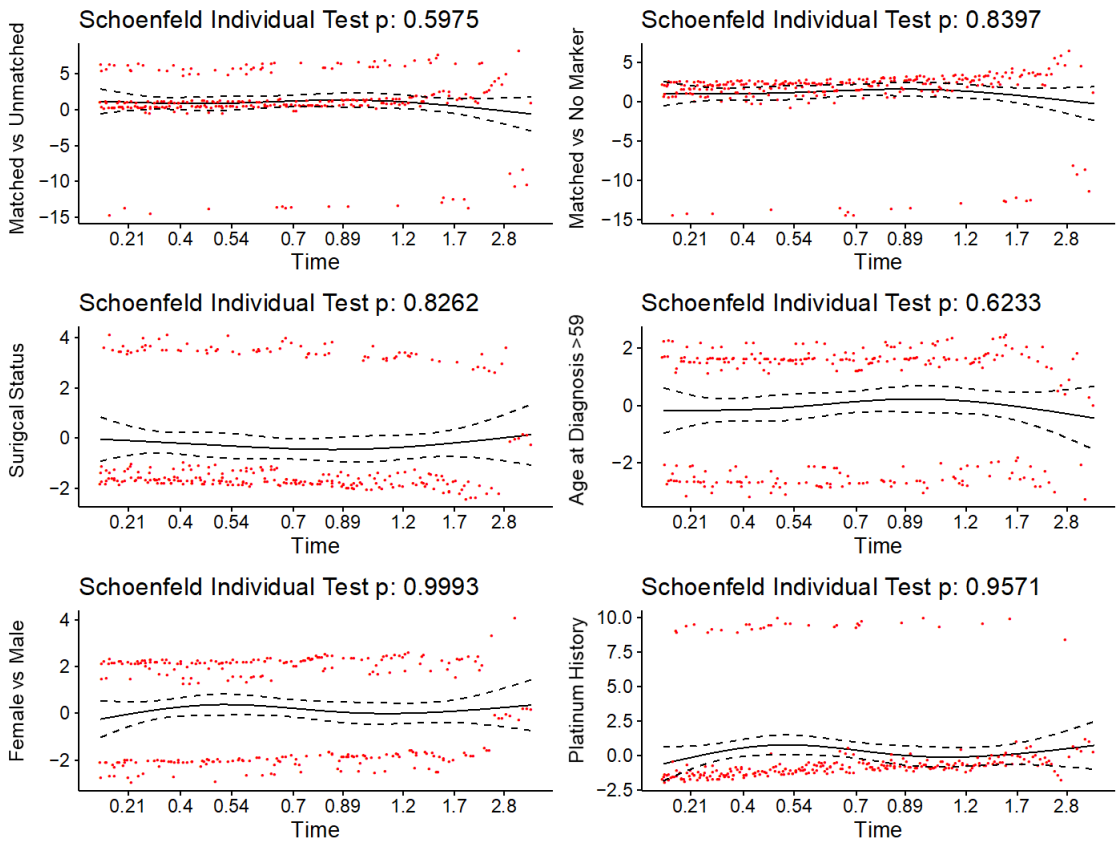
Supplemental Figure 1: Kaplan-Meier curves separated into patients who were originally diagnosed with advanced vs. resected disease. **A)** Patients who were diagnosed with advanced disease from the outset. **B)** Patients who were diagnosed with resectable disease, with the survival analysis initiated from the time of development of recurrent advanced/metastatic disease. **C)** Patients who were diagnosed with resectable disease, with the survival analysis initiated from the time of initial diagnosis. In each scenario, patients with actionable molecular alterations who received matched therapy had an improved mOS compared to patients with actionable alterations who did not receive patched therapy, and compared to patients with no actionable alterations.

Patient Baseline Characteristics	Fisher's Exact Test P-Value Molecularly-Matched vs Only Unmatched Therapy		Univariate Cox Model P-Value (HR [95% CI]) Baseline Characteristics Comparison	
	Advanced OS Cohort (n=189)	2nd Line OS Cohort (n=122)	Advanced OS Cohort (n=677)	2nd Line OS Cohort (n=410)
Female vs Male	0.1746	0.1227	0.7742 (0.97 [0.8-1.18])	0.1865 (0.85 [0.67-1.08])
Age <=59 vs Age >59	0.7347	0.7003	0.04718 (0.81 [0.66-1])	0.7459 (0.96 [0.76-1.22])
Advanced vs Resectable	0.2059	0.1228	0.3342 (1.11 [0.9-1.39])	0.09777 (1.25 [0.96-1.63])
Platinum Treated vs Naive	0.0035	0.2214	3.977e-07 (0.55 [0.44-0.69])	0.0552 (0.69 [0.47-1.01])
>=2 vs <2 Lines of Therapy	0.001237	N/A	3.132e-10 (0.49 [0.4-0.61])	N/A

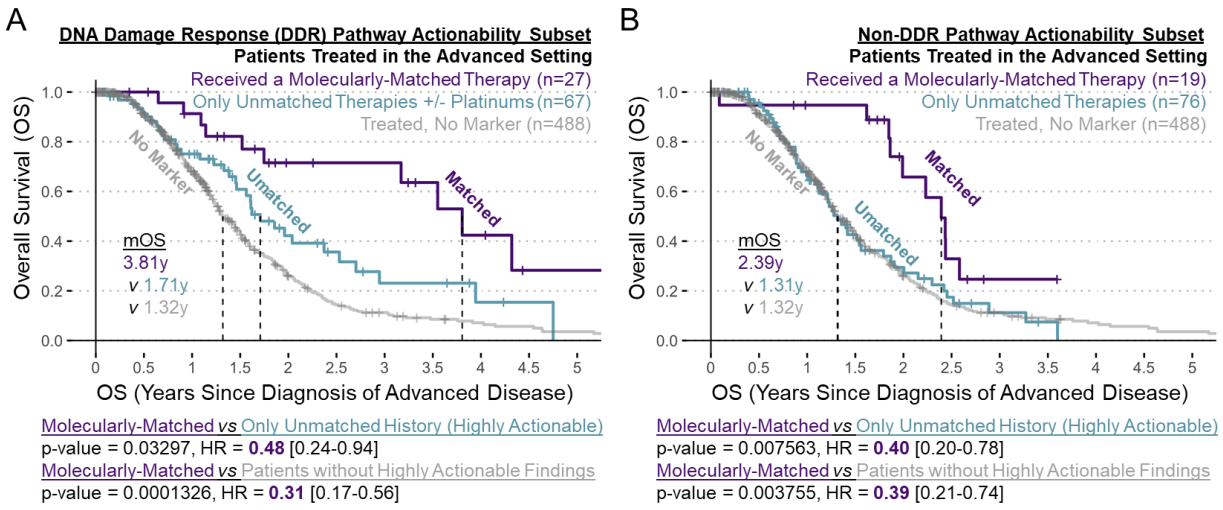
Supplementary Table 2: Statistical comparison of demographic subgroups. In the analysis of molecularly-matched versus unmatched cohorts. Fisher's exact test, and univariate cox model comparisons were made for key variables. No significant imbalances were observed across sex (p=0.1746), age at diagnosis (p=0.7347), or surgical status (p=0.2059). However, imbalances were noted with regards to exposure to platinum agents (p=0.0035), and with having received more than one line of therapy (p=0.001237).

Multivariate Model Contrast	Multivariate Cox Model P-Value (HR [95% CI])	
	Advanced OS Cohort (n=677)	2nd Line OS Cohort (n=410)
Molecularly-Matched vs **Only Unmatched Therapy**:	0.004759 (0.5 [0.31-0.81])	0.0003893 (0.39 [0.23-0.66])
Molecularly-Matched vs **No Actionable Marker:**	0.00006524 (0.4 [0.25-0.63])	0.000001085 (0.31 [0.19-0.5])
Female vs Male	0.7334 (0.97 [0.79-1.18])	0.2313 (0.86 [0.68-1.1])
Age <=59 vs Age >59	0.2450 (0.88 [0.72-1.09])	0.9511 (1.01 [0.79-1.28])
Advanced vs Resectable	0.3125 (1.12 [0.9-1.4])	0.0422 (1.32 [1.01-1.72])
Platinum Treated vs Naive	0.03035 (0.76 [0.59-0.97])	0.2273 (0.79 [0.54-1.16])
>=2 vs <2 Lines of Therapy	0.000003132 (0.57 [0.45-0.72])	N/A

Supplementary Table 3: Multivariate Cox Regression Model. To further assess the impact of potentially confounding factors on these results, we evaluated a multivariate cox regression model taking into account: sex, age at diagnosis, surgical status, and platinum exposure The model demonstrated that the significance of these contrasts comparing patients who received a matched therapies to the other groups were relatively unchanged in both sets of analyses (mOS from advanced diagnosis and from initiation of second-line).



Supplementary Figure 2: Schoenfeld Tests: Proportionality of hazards was assessed for each variable and Schoenfeld residuals were visually inspected for potential time-variant biases and none were considered significant based on a p-value threshold of 0.05. A significance threshold for p-values was arbitrarily set to 0.05 for all statistical tests.



Supplemental Figure 3: Kaplan-Meier curves for patients whose tumors harbored either actionable alterations within the DDR pathway or within other pathways. A) A mOS benefit was seen in patients who received DDR inhibitors (including PARP inhibitors) that were molecularly-matched to actionable alterations within the DDR pathway versus those who did not receive a DDR inhibitor. **B)** A mOS benefit was seen in patients whose tumors harbored alterations beyond the scope of the DDR pathway and who received a molecularly-matched therapy.