

Encyclopedic Tumor Analysis (ETA) Guided Combination Regimens of Hormone Receptor Antagonists with Other Systemic Agents for Treatment of Refractory Cancers

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Conflict of Interest:
Datar Cancer Genetics Limited offers commercial services in the domain of oncology.

BACKGROUND

- Hormone and Growth Factor Receptors (HR), e.g., AR, ER, PR, HER2 are involved in pathogenesis of cancers,
- HR antagonists administered as both monotherapy as well as in combinations with selected cytotoxic or targeted agents.
- In the SHIVA trial, label-agnostic monotherapy with HR antagonists yielded dismal results.

RATIONALE

- Encyclopedia Tumor Analysis (ETA) is an integrational multi-analyte evaluation of tumor features using DNA, RNA, proteins and viable tumor derived cells (TDCs).
- ETA identifies latent vulnerabilities of the tumor and can guide patient-specific combination regimens for tandem-targeting of tumor vulnerabilities.

APPROACH

- 37 patients with advanced, refractory solid organ cancers which had progressed following ≥2 prior systemic lines,
- Patients received personalized combination regimens with HR antagonists based on ETA,
- Treatment response was determined radiologically. (Objective Response Rate, ORR and Disease Control Rate, DCR).

DEMOGRAPHICS

Table 1. Study Cohort

Cancer Type	Number
Breast	15
Ovarian	5
Liver	3
Kidney	3
Cervical	2
Pancreatic	2
Colorectal	1
Head and Neck	1
Lung	1
Melanoma	1
NET	1
Prostate	1
Sarcoma	1

11 males + 26 females. Median age: 57 years (Range 28-72).

Figure 1. Extent of Disease-Metastases.

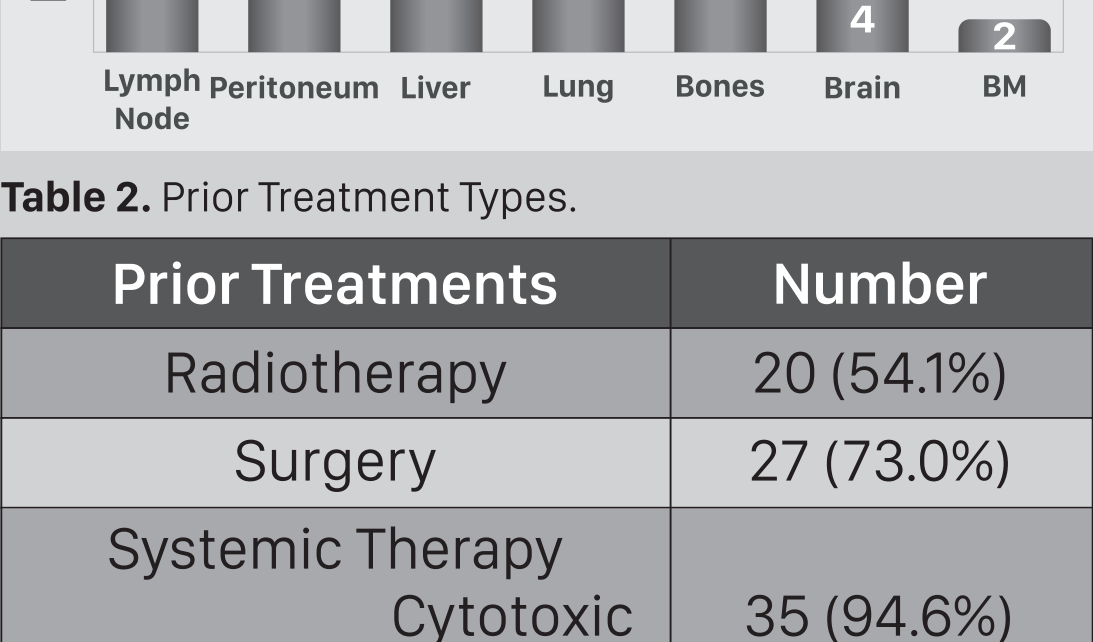


Table 2. Prior Treatment Types.

Prior Treatments	Number
Radiotherapy	20 (54.1%)
Surgery	27 (73.0%)
Systemic Therapy	
Cytotoxic	35 (94.6%)
Targeted	14 (37.8%)
Endocrine	7 (18.9%)

Table 3. Number of Metastatic Sites.

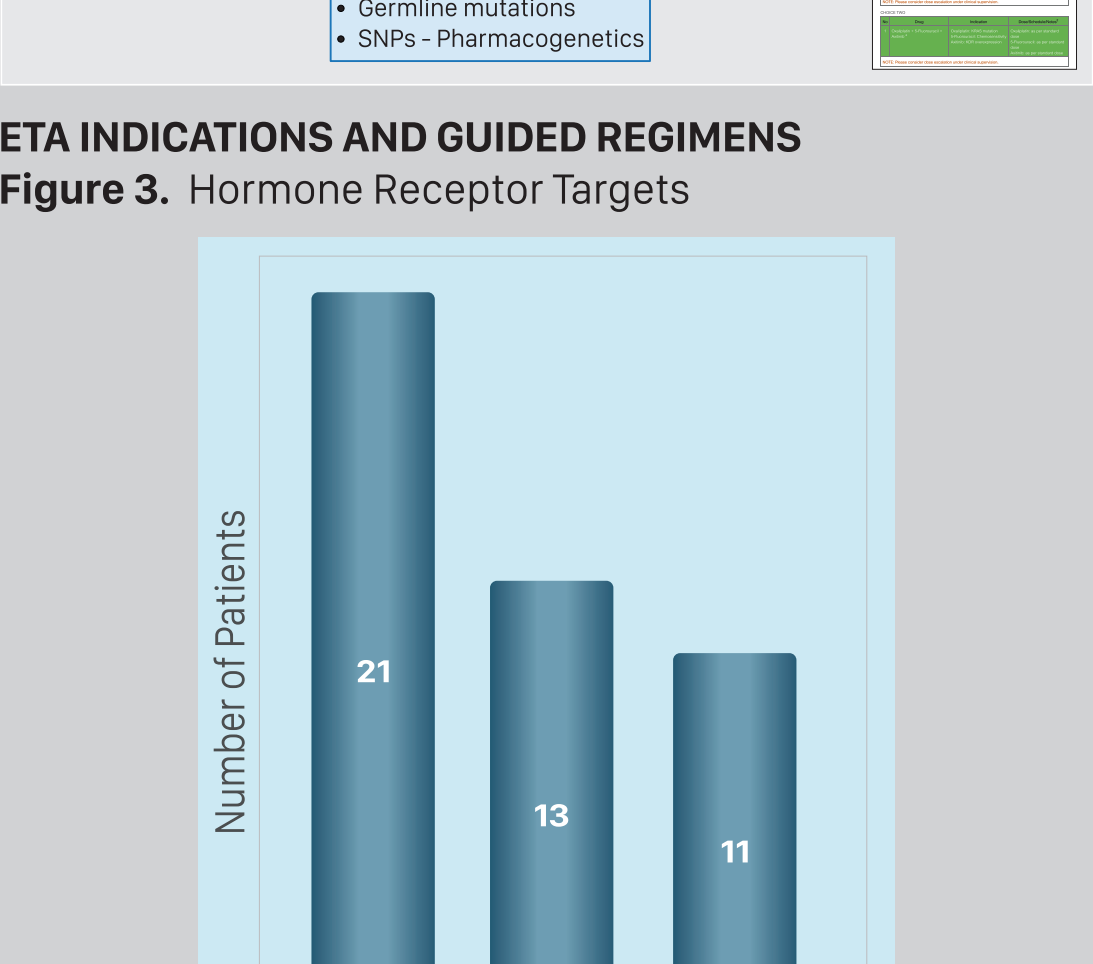
Metastatic Sites	Number
Minimum	1
Maximum	12
Median	3

Table 4. Prior Treatment Lines.

Prior Lines	Systemic	All
Minimum	1	1
Maximum	14	17
Median	3	4

ENCYCLOPEDIA TUMOR ANALYSIS

Figure 2. Overview of Analytes and Analyses in ETA.



ETA INDICATIONS AND GUIDED REGIMENS

Figure 3. Hormone Receptor Targets

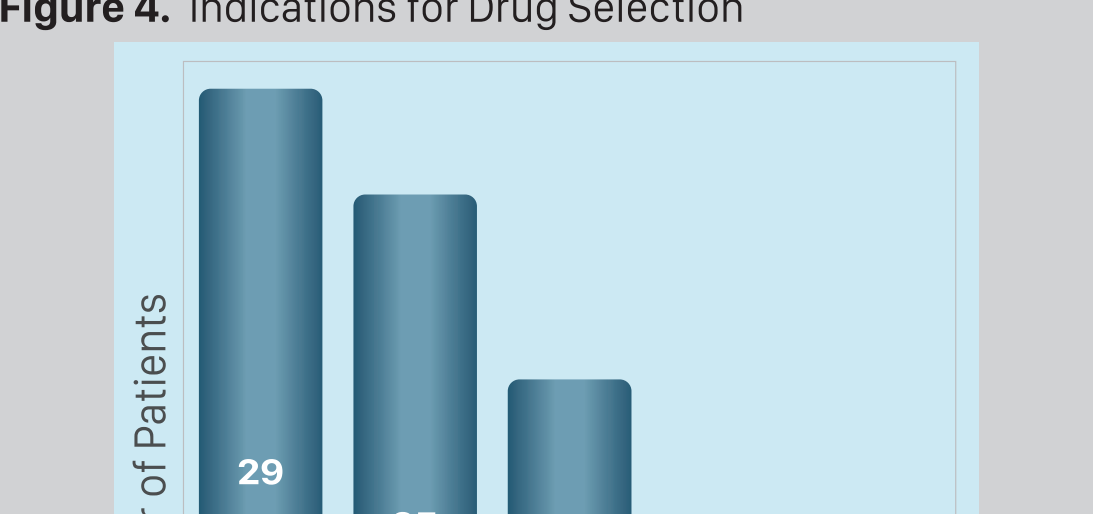
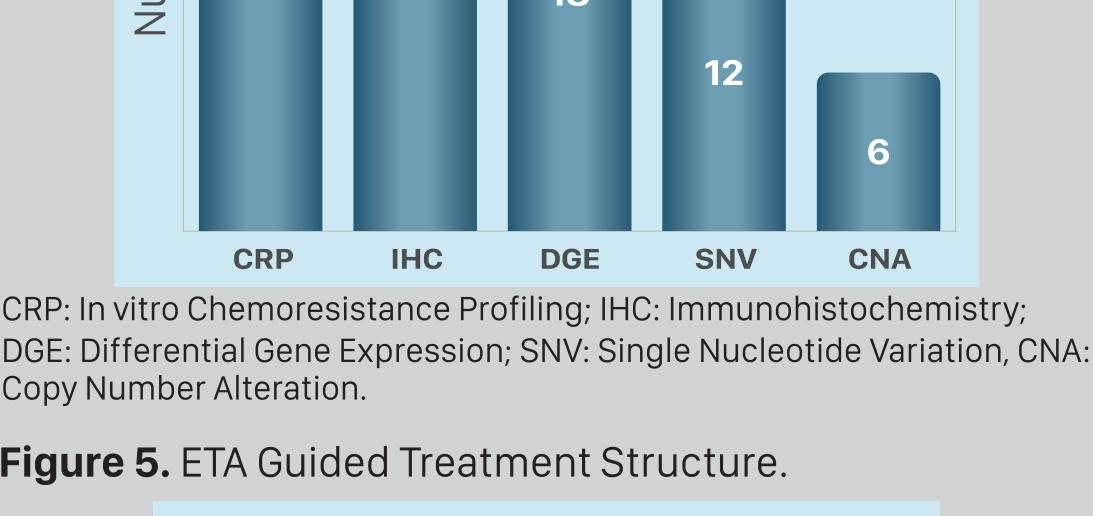
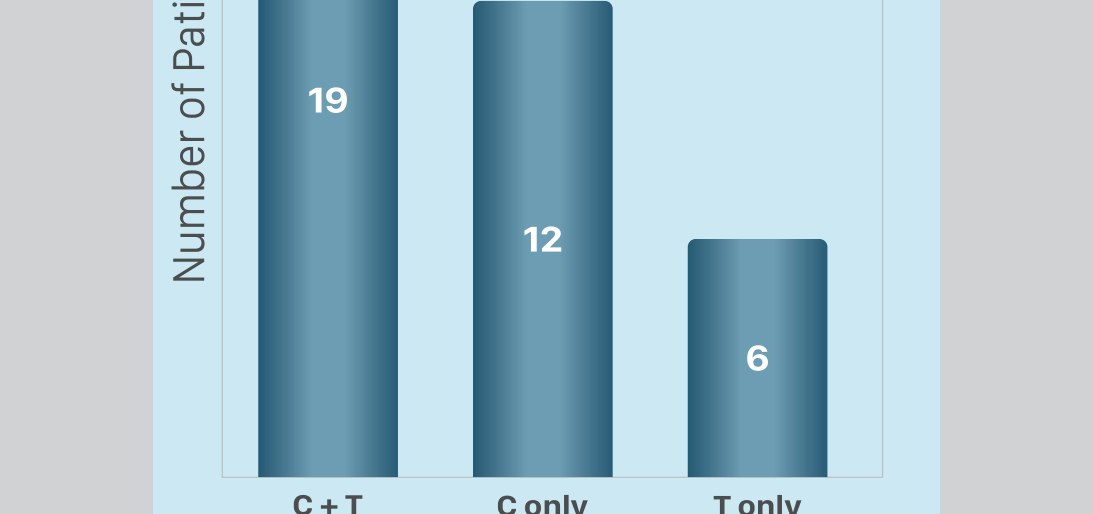


Figure 4. Indications for Drug Selection



CRP: In vitro Chemoresistance Profiling; IHC: Immunohistochemistry; DGE: Differential Gene Expression; SNV: Single Nucleotide Variation, CNA: Copy Number Alteration.

Figure 5. ETA Guided Treatment Structure.

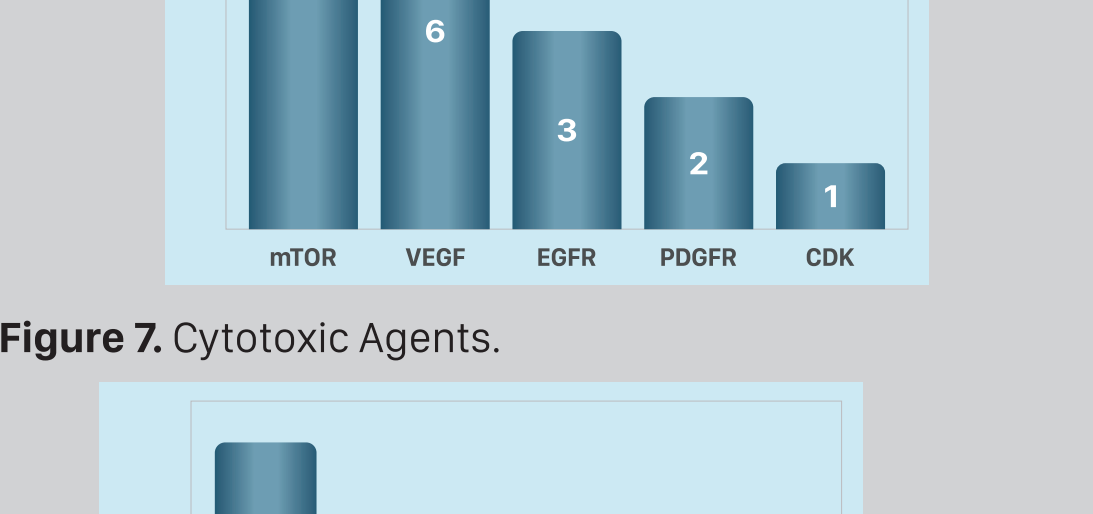


C: Cytotoxic Drugs; T, Targeted Drugs; C+T: Cytotoxic + Targeted Drugs

Figure 6. Profile of Targeted Agents.



Figure 7. Cytotoxic Agents.



TREATMENT RESPONSE

Figure 8. Objective Response Rate and Disease Control Rate.

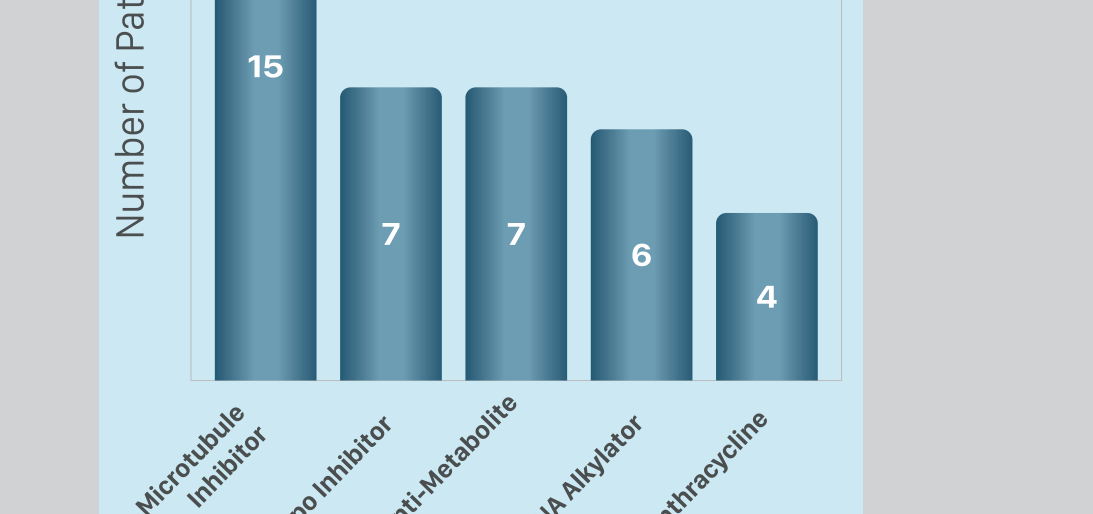


Figure 9. Waterfall Chart of Change in Tumor Size in Response to ETA Guided Regimens.

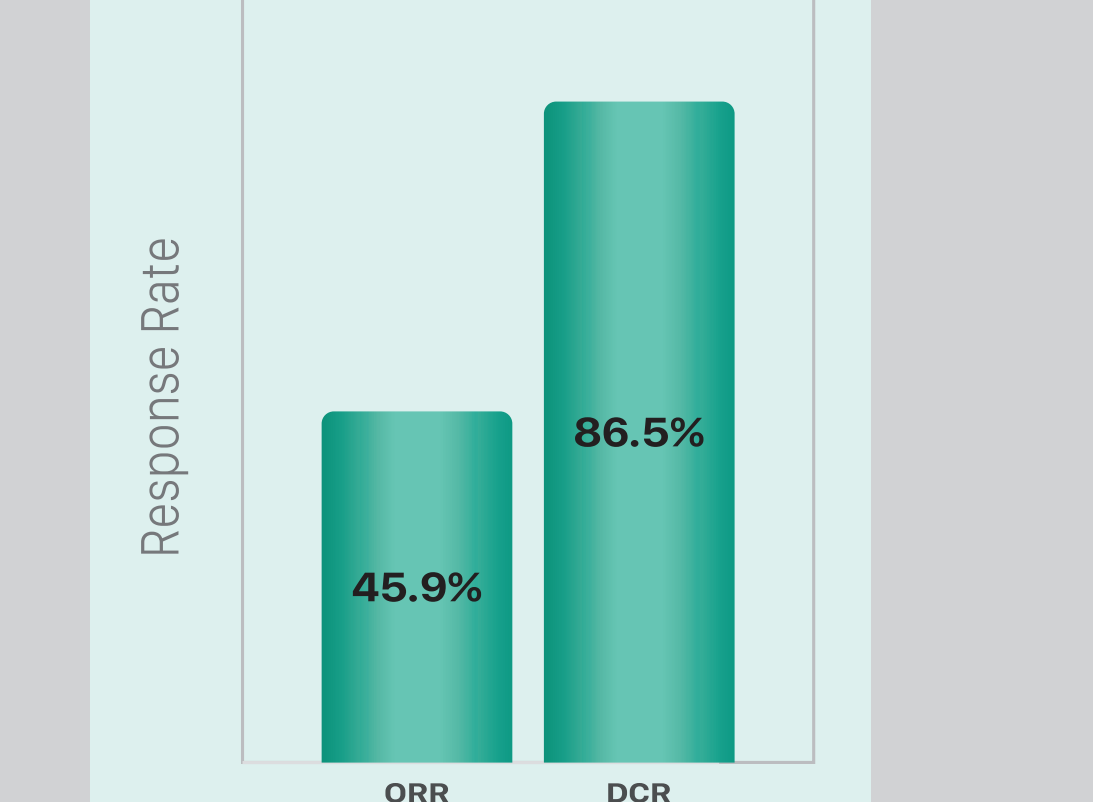


Figure 10. Progression Free Survival.

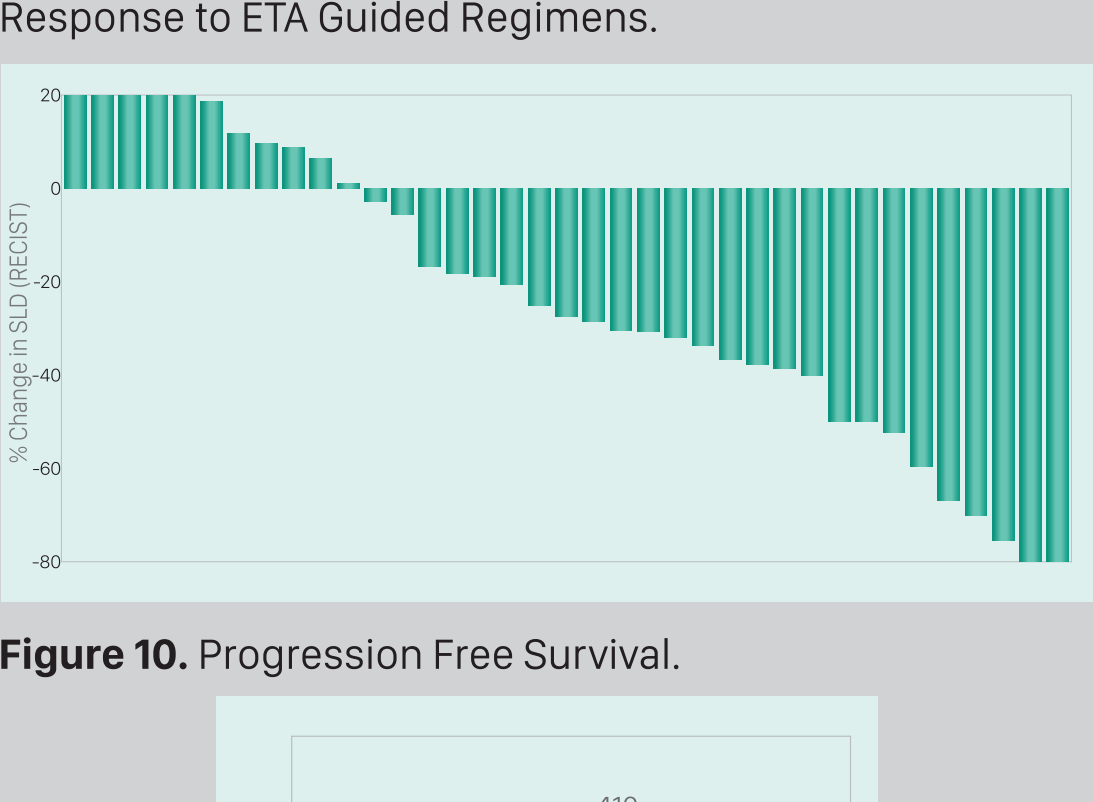
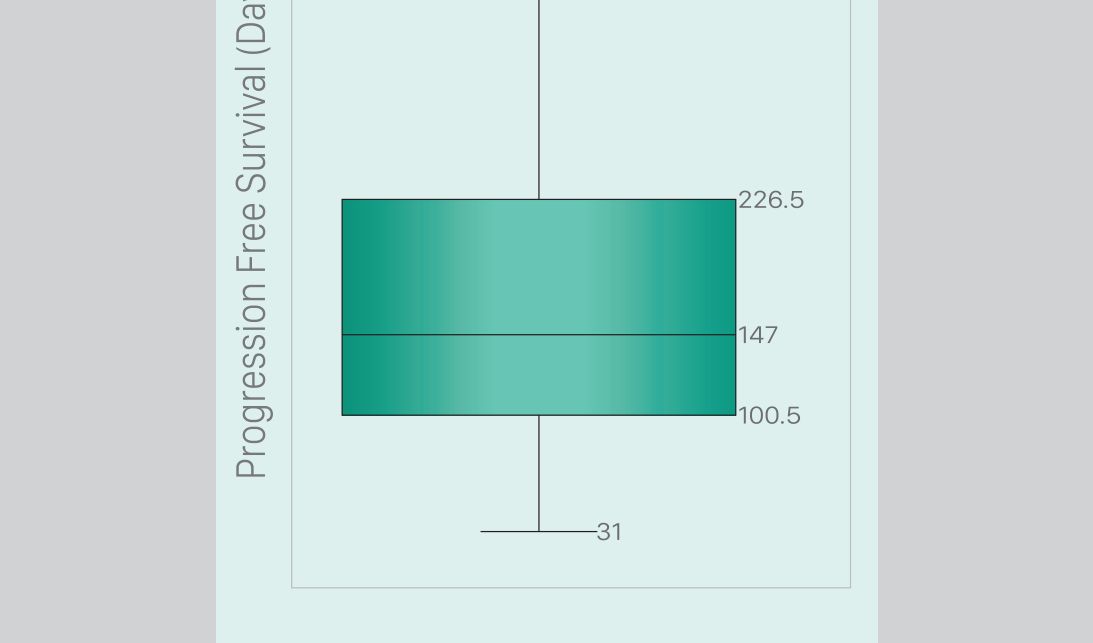


Figure 11. Kaplan Meier Curve of Progression-Free Survival.



FINDINGS

- Partial response (PR) was observed in 17 patients (ORR= 45.9%),
- Stable Disease (SD) was observed in 15 patients (DCR= 86.5%),
- Median PFS was 147 days.
- No Grade IV therapy-related AE (AEs) or any treatment related deaths.

CONCLUSION

ETA-guided combination regimens with HR antagonists offer a viable and efficient strategy in advanced refractory malignancies and outperform mTOR inhibitor monotherapy.