

# mTOR Inhibitors in Combination Regimens Guided by Encyclopedic Tumor Analysis (ETA) Show Superior Outcomes Compared to Monotherapy in Refractory Cancers

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## Conflict of Interest:

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

## BACKGROUND

- Though mTOR inhibition is a sound strategy for cancer management, anti-mTOR monotherapies have not shown meaningful benefits.
- Deep interrogation of the tumor can reveal indications for combination treatments with mTOR inhibitors in a label- and organ-agnostic manner.

## 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

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

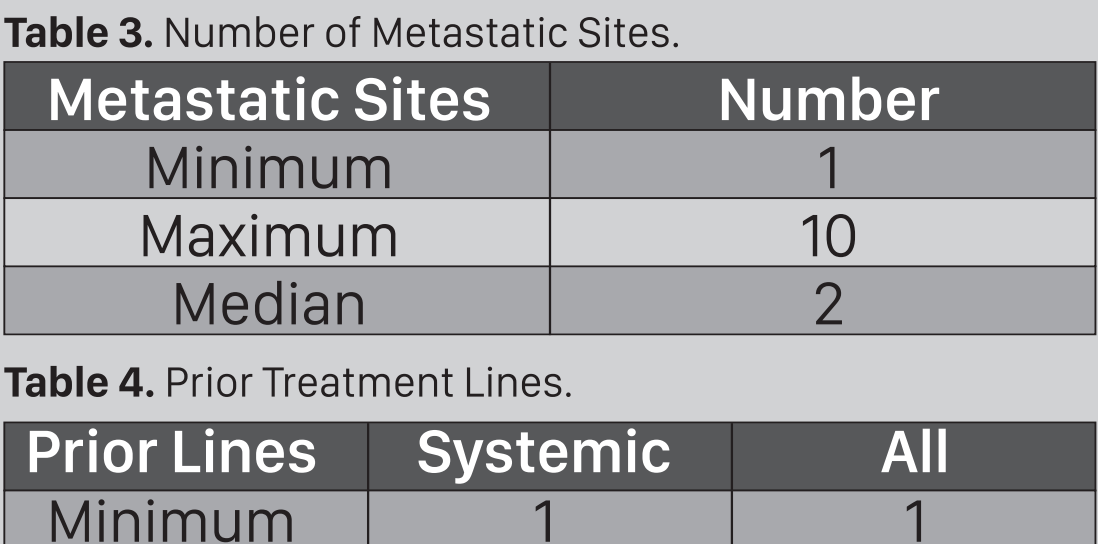
## DEMOGRAPHICS

**Table 1.** Study Cohort

Cancer Type	Number
Breast	16
Head and Neck	5
Ovarian	4
Lung	3
Cervical	2
Colorectal	2
Hepatobiliary	2
Esophageal	1
Gastric	1
Kidney	1
Melanoma	1
Pancreatic	1
Prostate	1
Sarcoma	1
Testicular	1

16 males + 26 females. Median age: 54 years (Range 22–68)

**Figure 1.** Extent of Disease–Metastases.



**Table 2.** Prior Treatment Types.

Prior Treatments	Number
Radiotherapy	19 (39.6%)
Surgery	28 (66.7%)
Systemic Therapy	
Cytotoxic	42 (100.0%)
Targeted	14 (33.3%)
Endocrine	8 (19.1%)

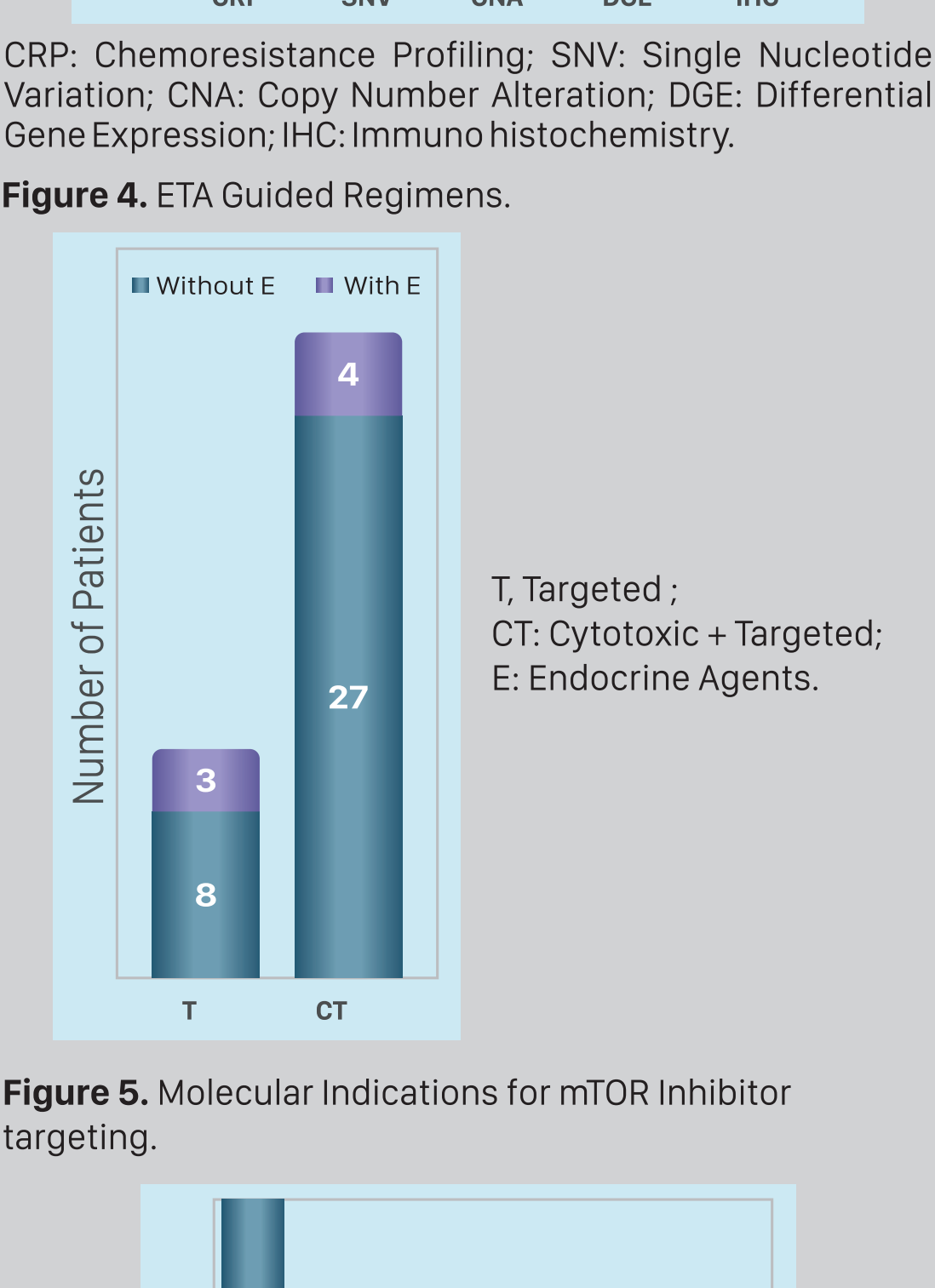
**Table 3.** Number of Metastatic Sites.

Metastatic Sites	Number
Minimum	1
Maximum	10
Median	2

**Table 4.** Prior Treatment Lines.

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

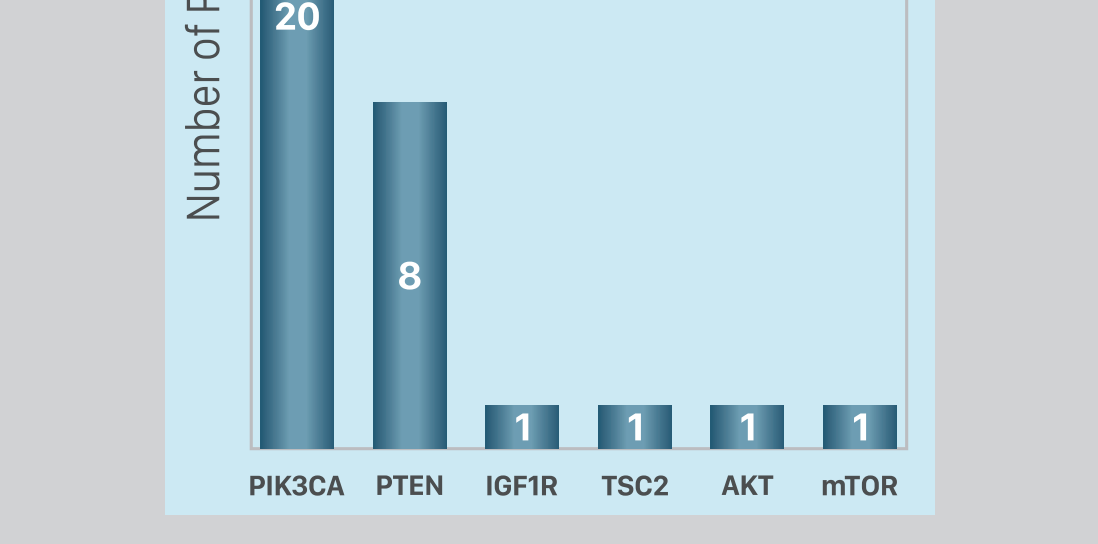
## ENCYCLOPEDIC TUMOR ANALYSIS



**Figure 2.** Overview of Multi-Analyte Investigations in ETA

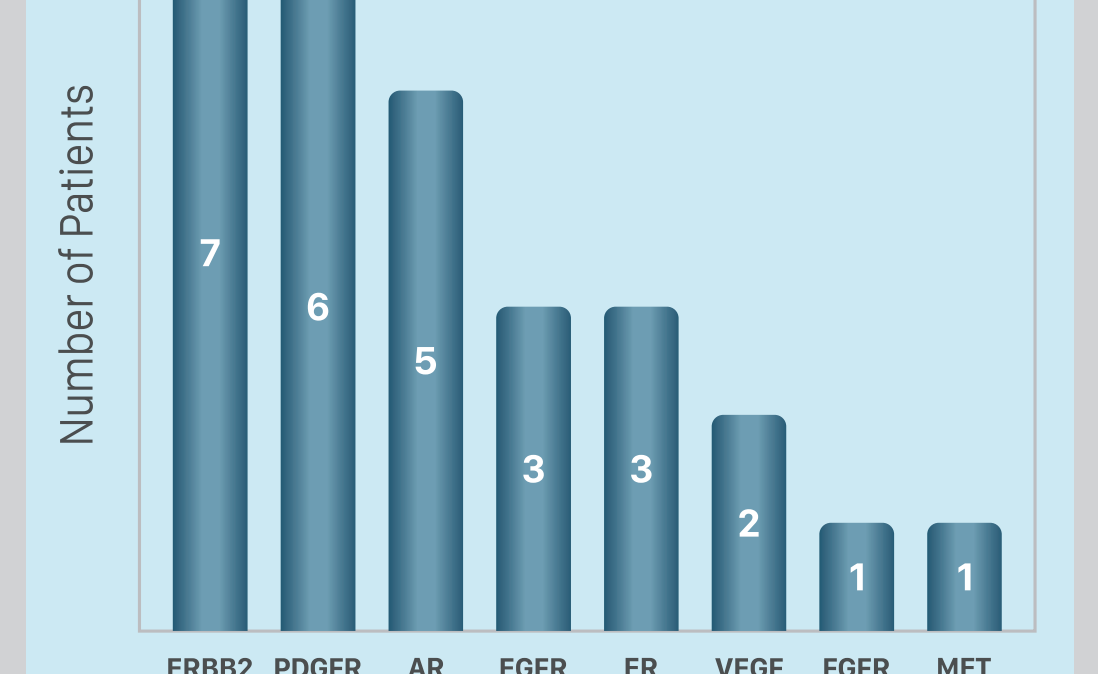
## ETA INDICATIONS AND GUIDED REGIMENS

**Figure 3.** ETA Indications.

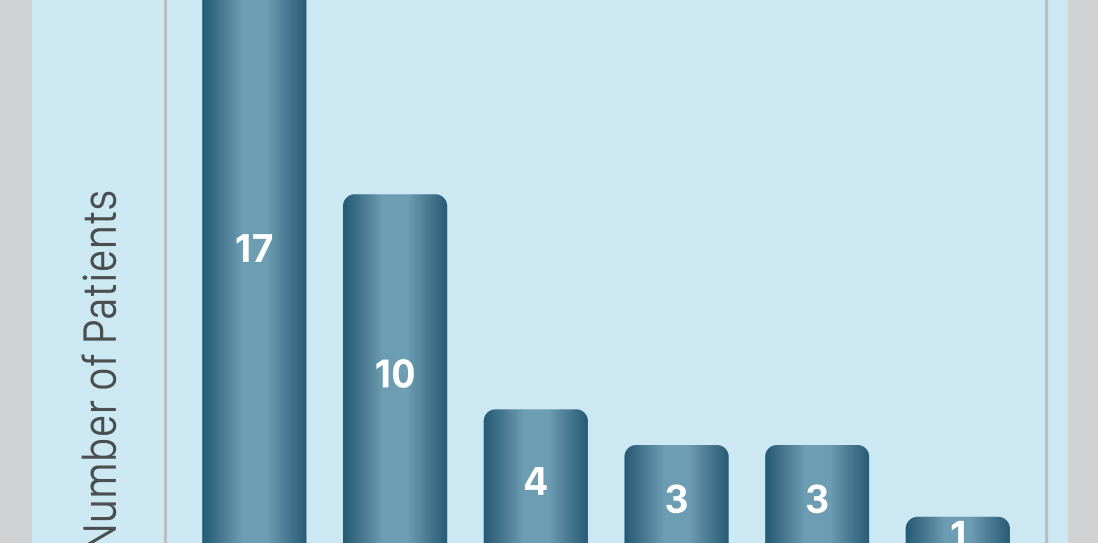


CRP: Chemoresistance Profiling; SNV: Single Nucleotide Variation; CNA: Copy Number Alteration; DGE: Differential Gene Expression; IHC: Immuno histochemistry.

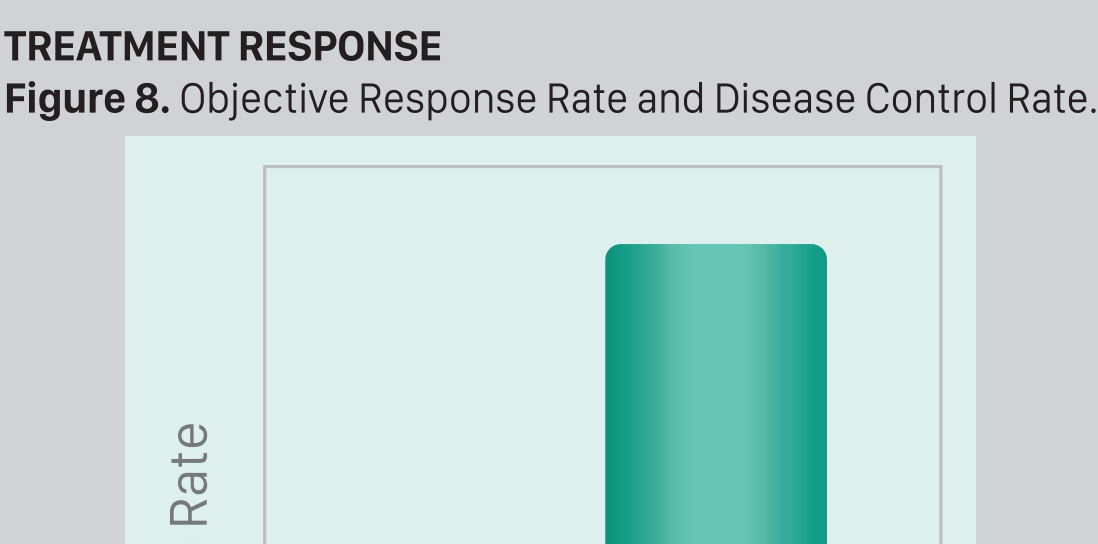
**Figure 4.** ETA Guided Regimens.



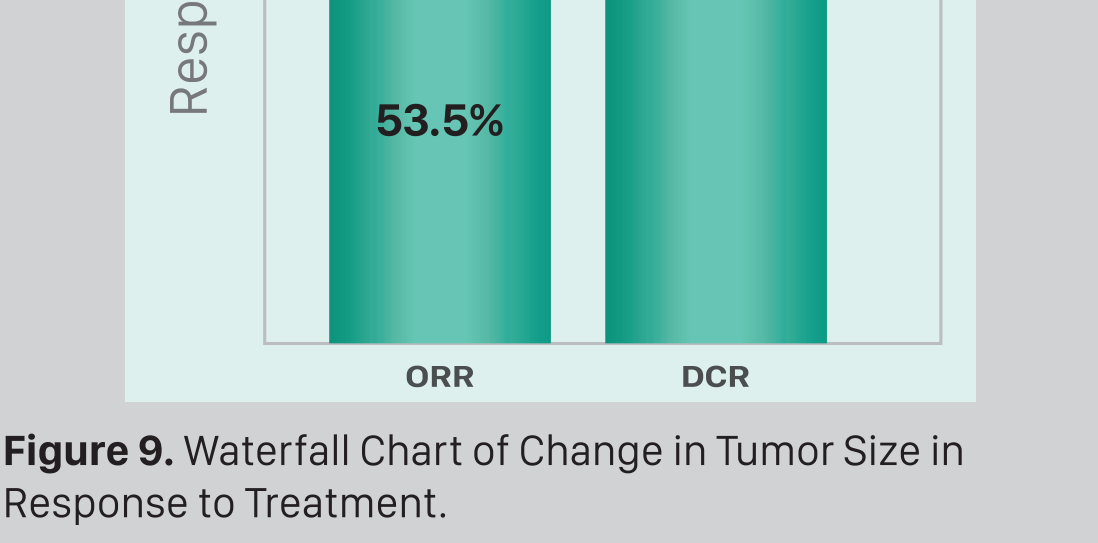
**Figure 5.** Molecular Indications for mTOR Inhibitor targeting.



**Figure 6.** Molecular Indications for Targeted Inhibitors and Endocrine Antagonists.

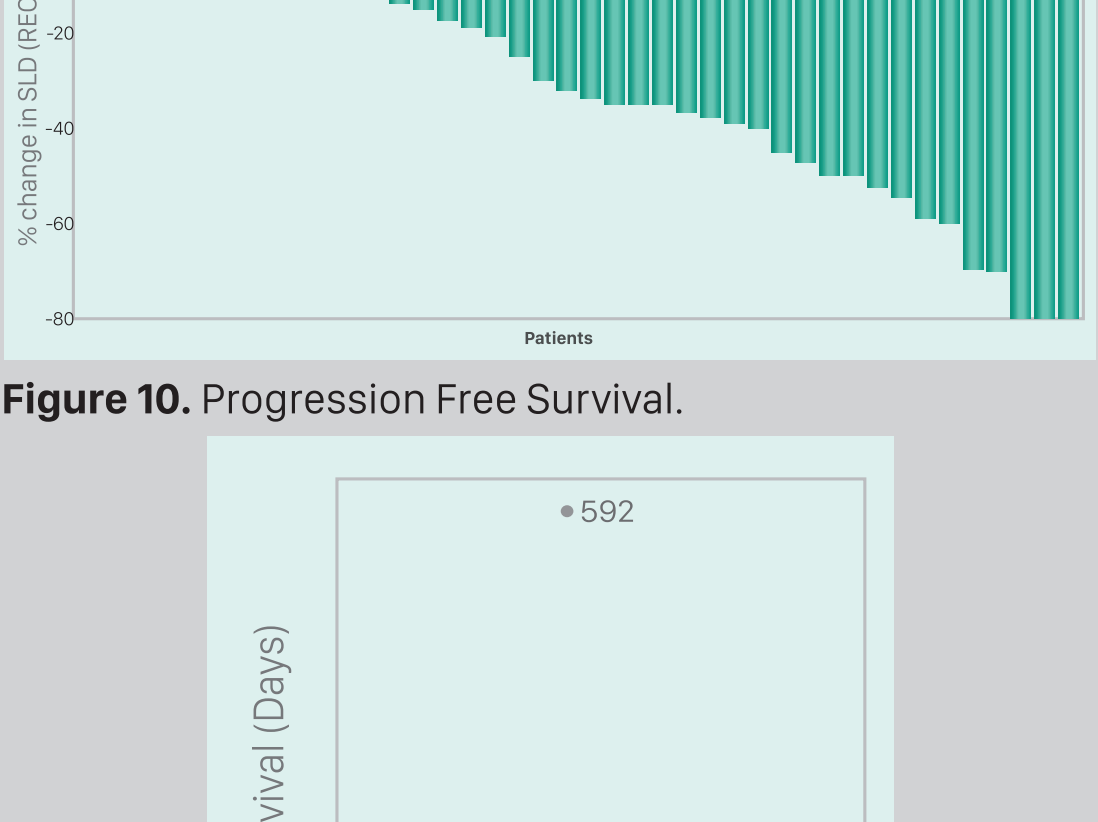


**Figure 7.** Cytotoxic Agents.

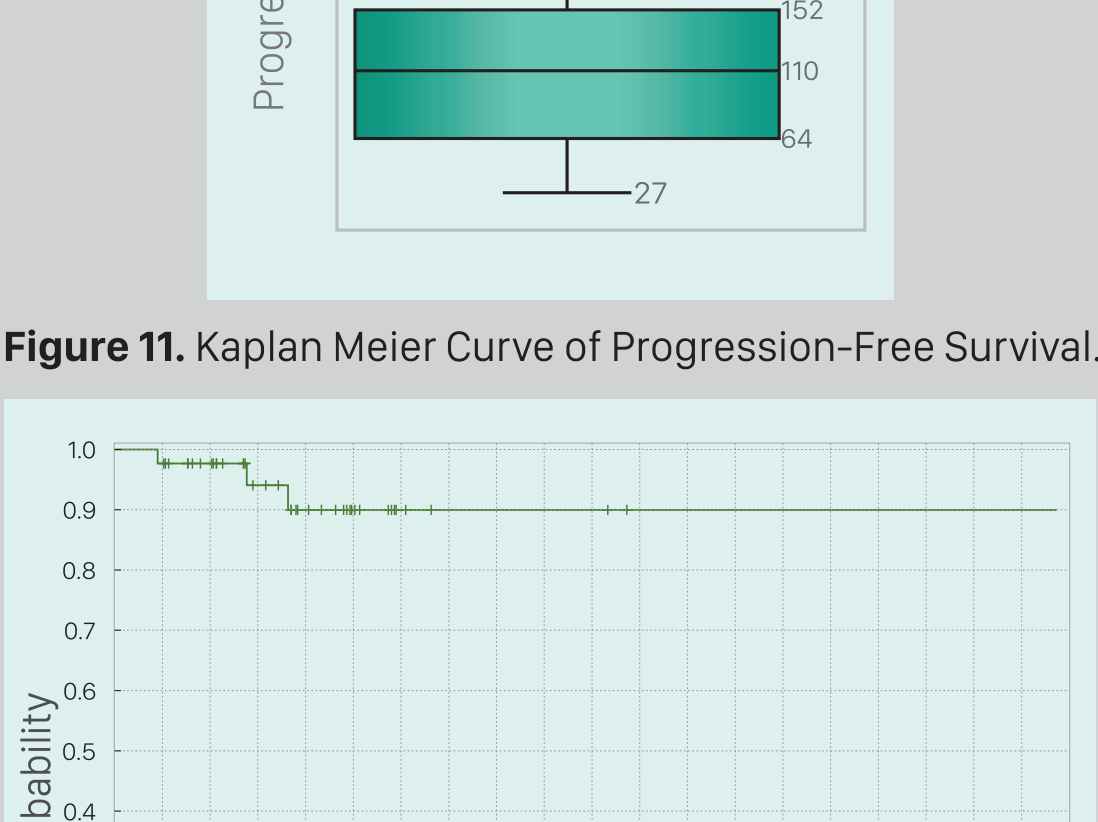


## TREATMENT RESPONSE

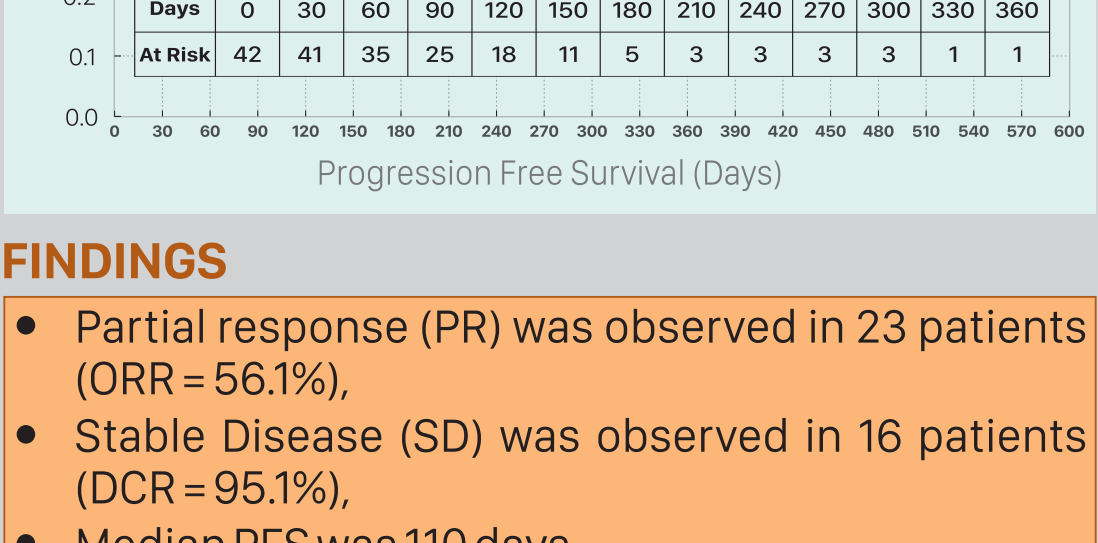
**Figure 8.** Objective Response Rate and Disease Control Rate.



**Figure 9.** Waterfall Chart of Change in Tumor Size in Response to Treatment.



**Figure 10.** Progression Free Survival.



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

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