

INTRODUCTION

- Immunotherapy resistance is an unmet clinical need in NSCLC.
- PCSK9 is an immuno-inhibitory therapeutic target in preclinical models.
- First-in-class proof of principle clinical trial evaluating the clinical activity and safety of anti-PCSK9 (alirocumab) plus anti-PD1 (cemiplimab) in immunorefractory metastatic NSCLC.
- Preliminary efficacy findings in the first 40/60 patients are reported.

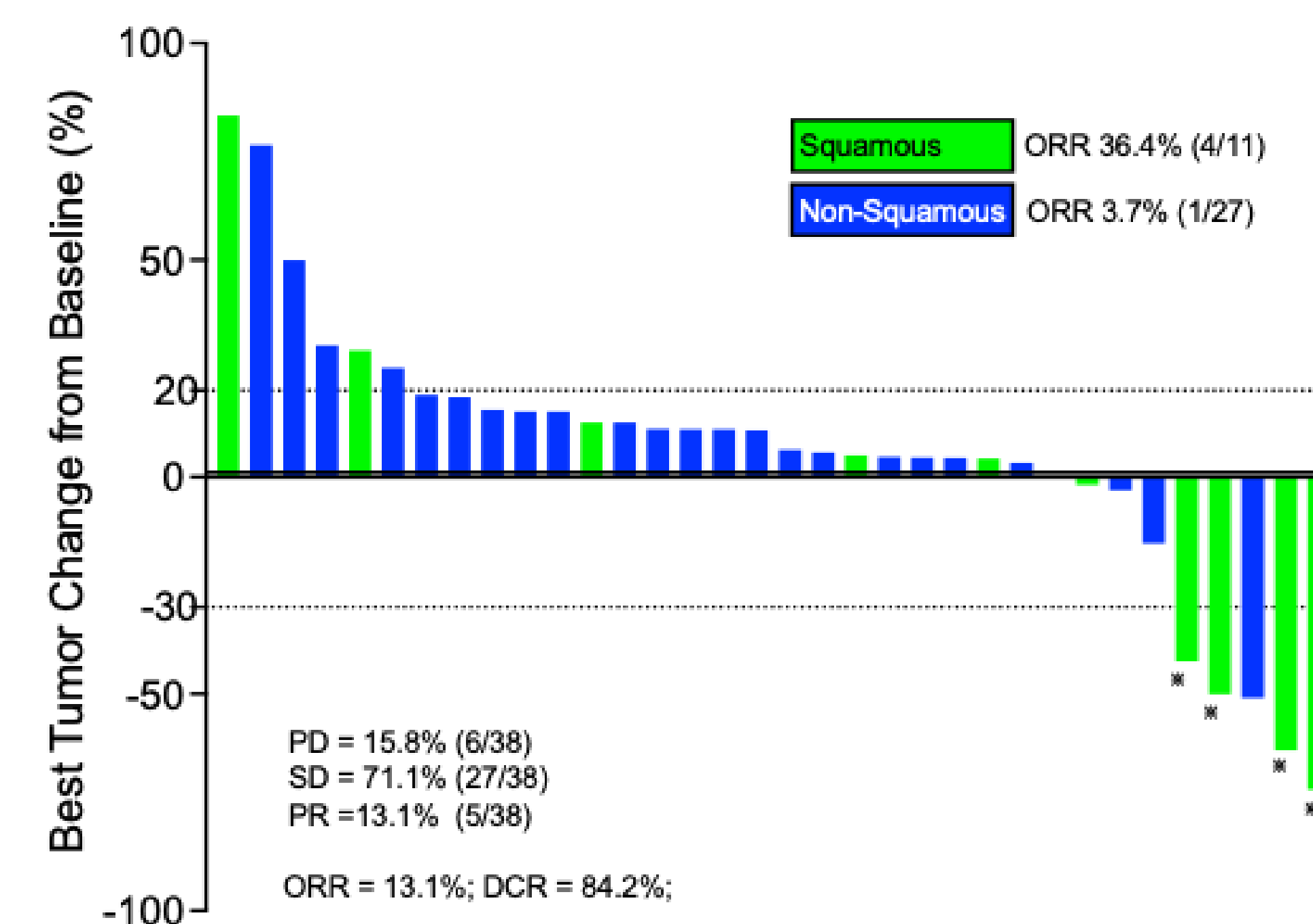
METHODS

Design:

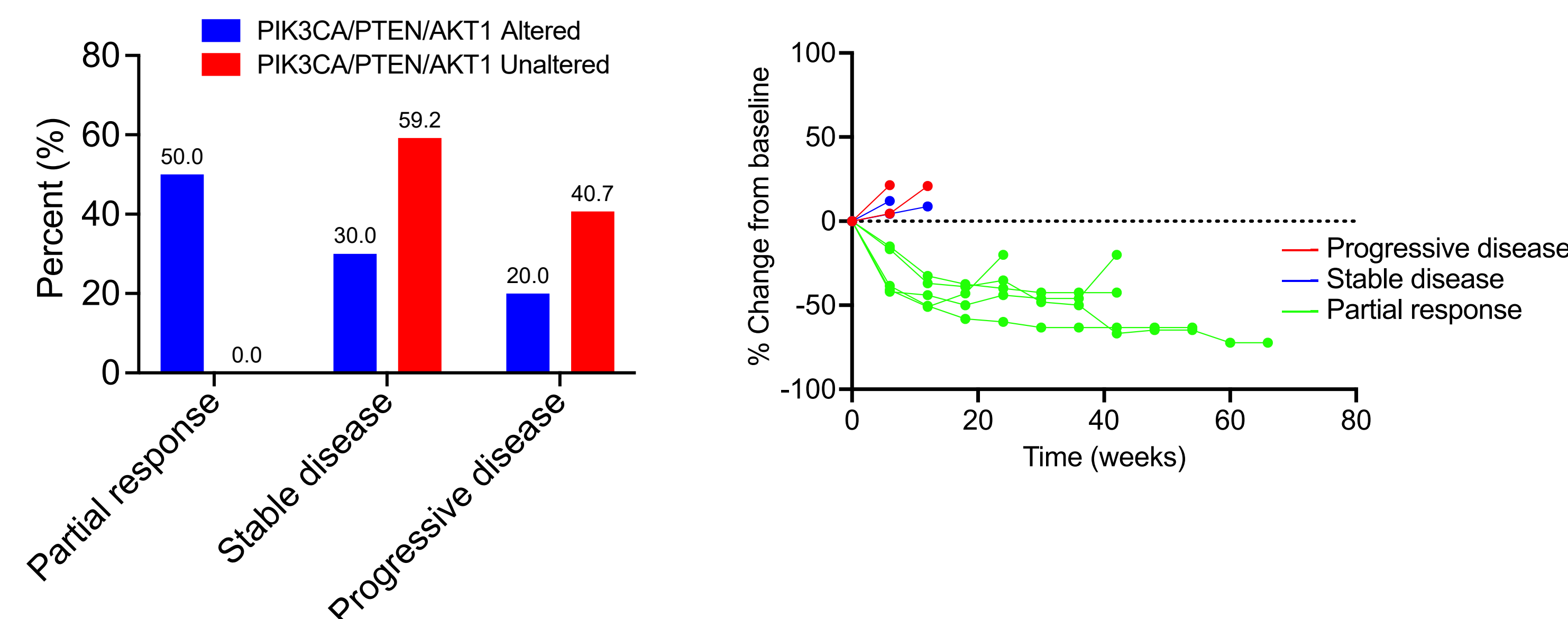
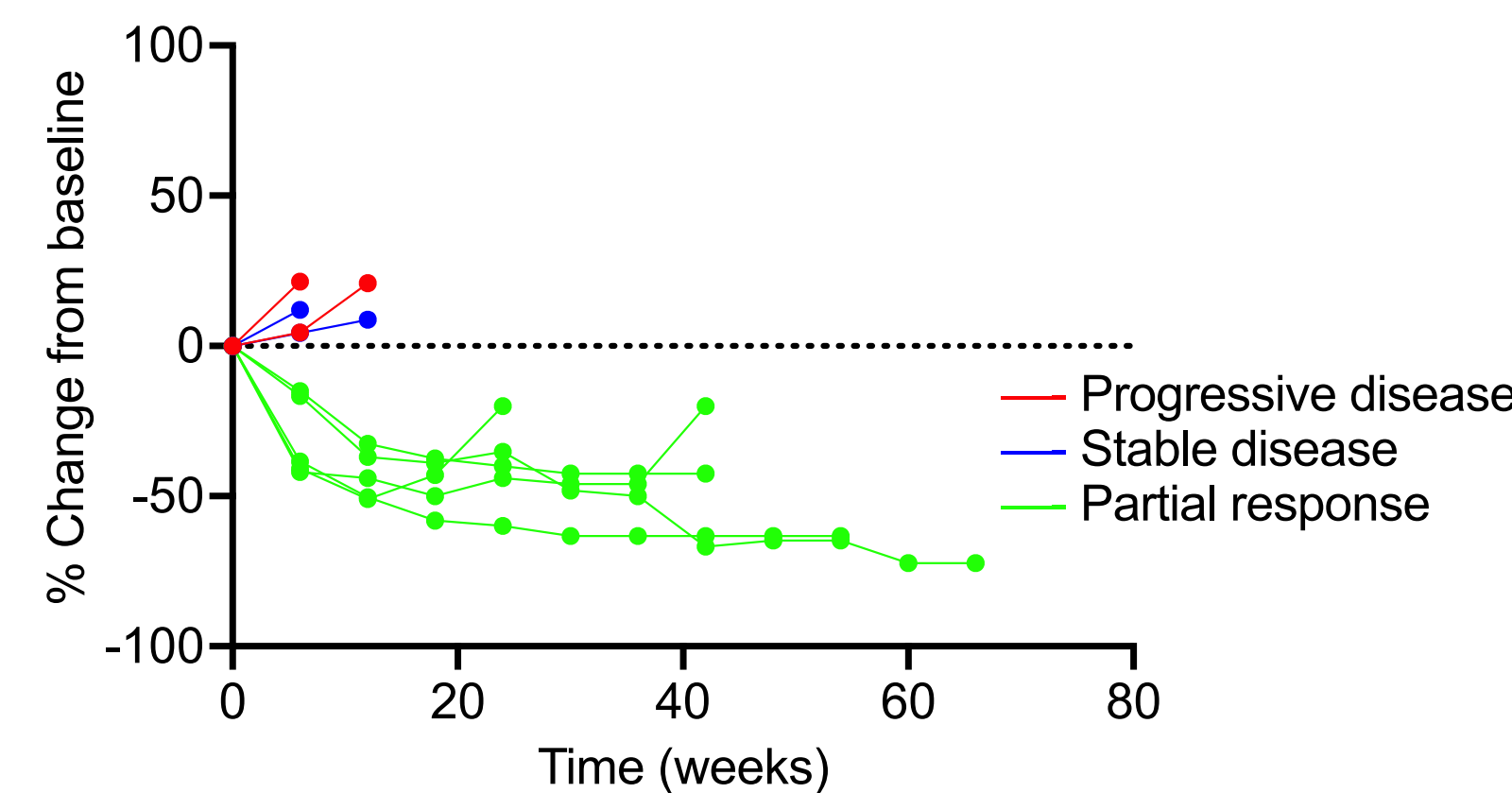
- Phase 2, multi-institutional single arm trial.
- Sites:
 - Duke Cancer Institute
 - Moffitt Cancer Center
- Evaluate the clinical activity and safety of alirocumab (PCSK9 inhibitor) plus cemiplimab (anti-PD1 antibody) in metastatic NSCLC who had progressed on prior immune checkpoint blockade.
- Primary endpoint: ORR
- Secondary efficacy endpoints:
 - PFS, OS, DOR, DCR
- Correlative objectives:
 - Biomarkers of response
- Planned sample size: 60
- ClinicalTrials.gov ID NCT05553834
- Study approved by Duke IRB

RESULTS

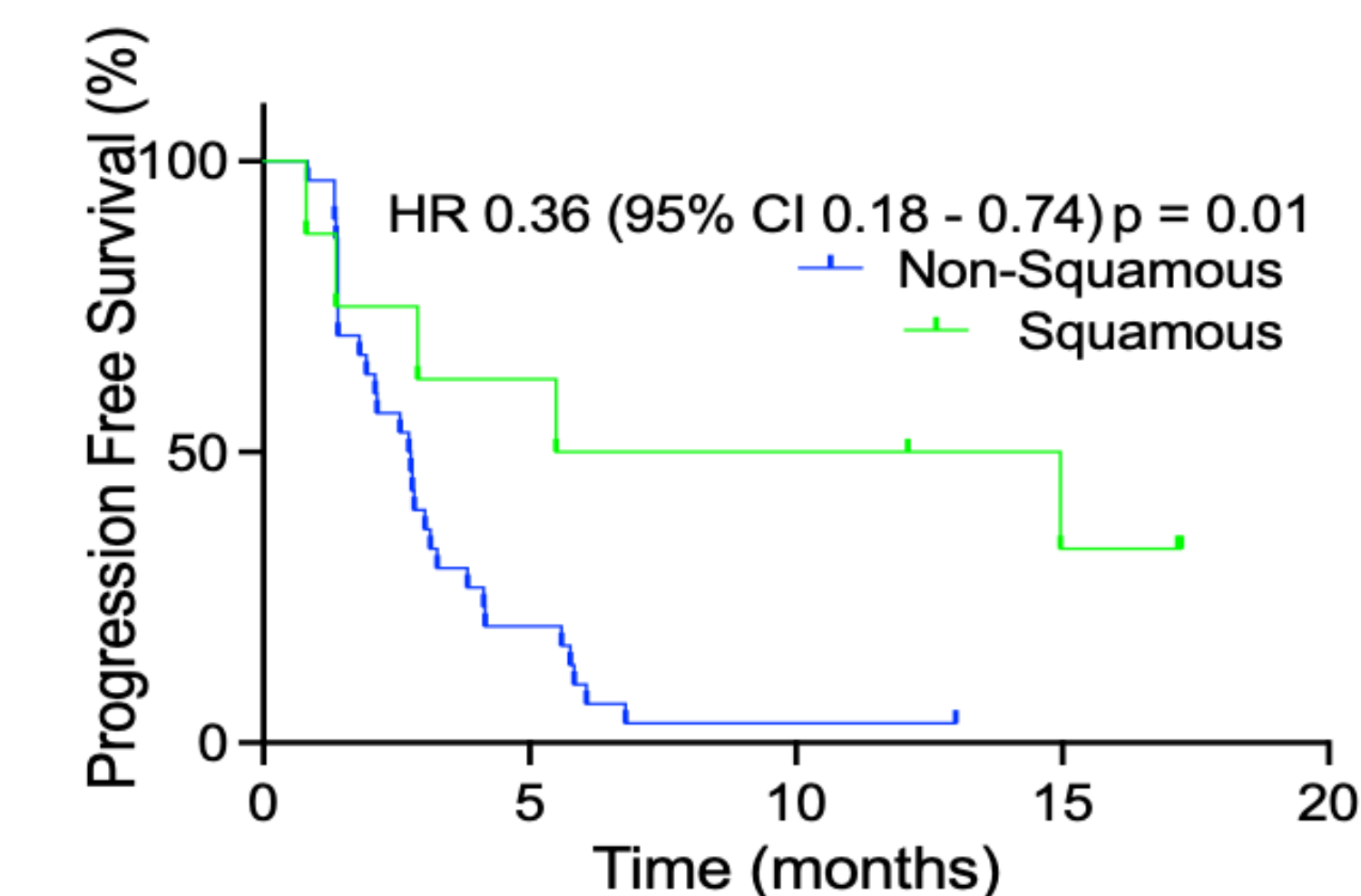
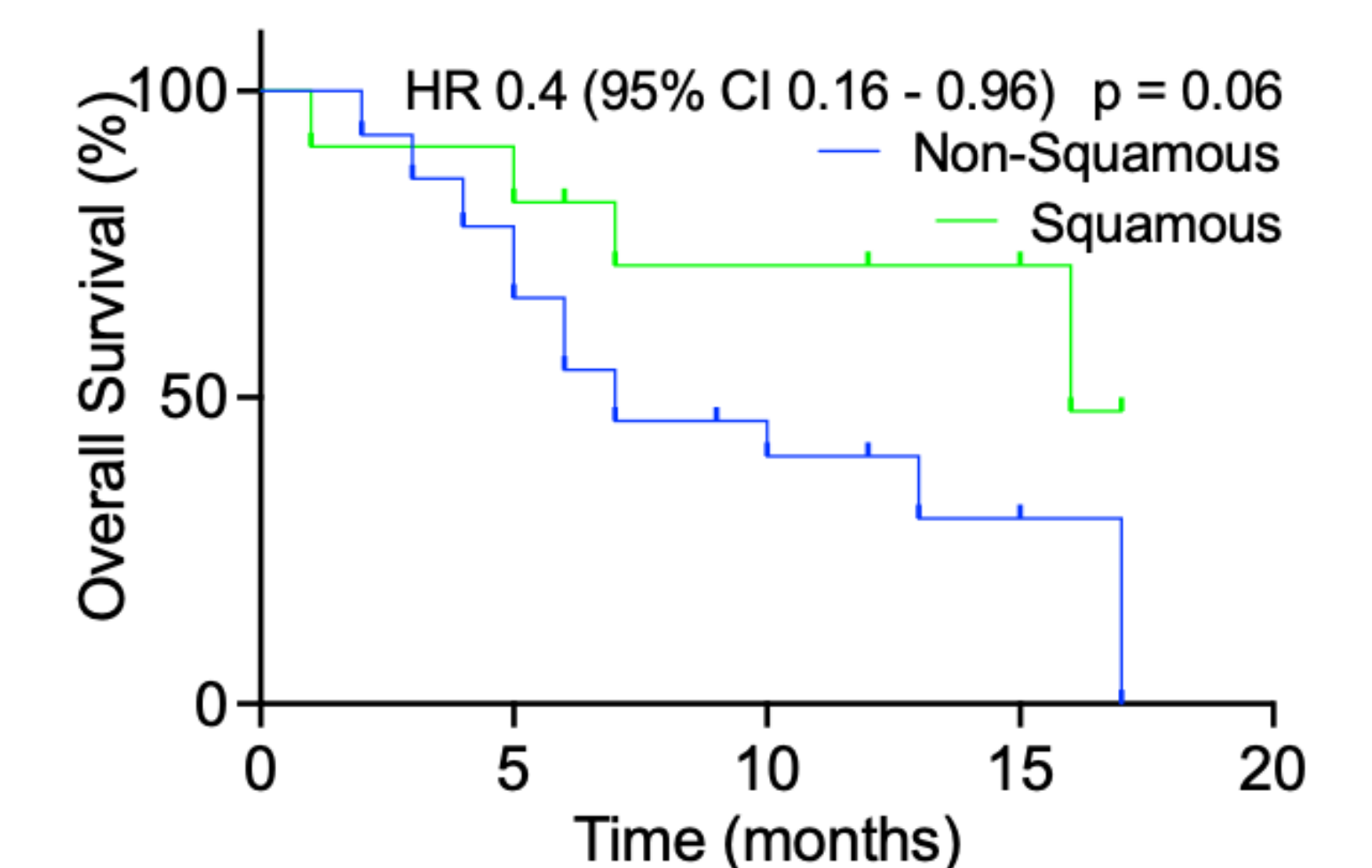
Alirocumab + Cemiplimab demonstrated efficacy in immunorefractory NSCLC. In the evaluable patients (n= 38), ORR was 36.4% (4/11) in squamous and 3.7% (1/27) in non-squamous histology.



All responders (5/5) had alterations in PIK3CA, AKT1 or PTEN and had durable responses. Altered (n = 10); Unaltered (n= 28)

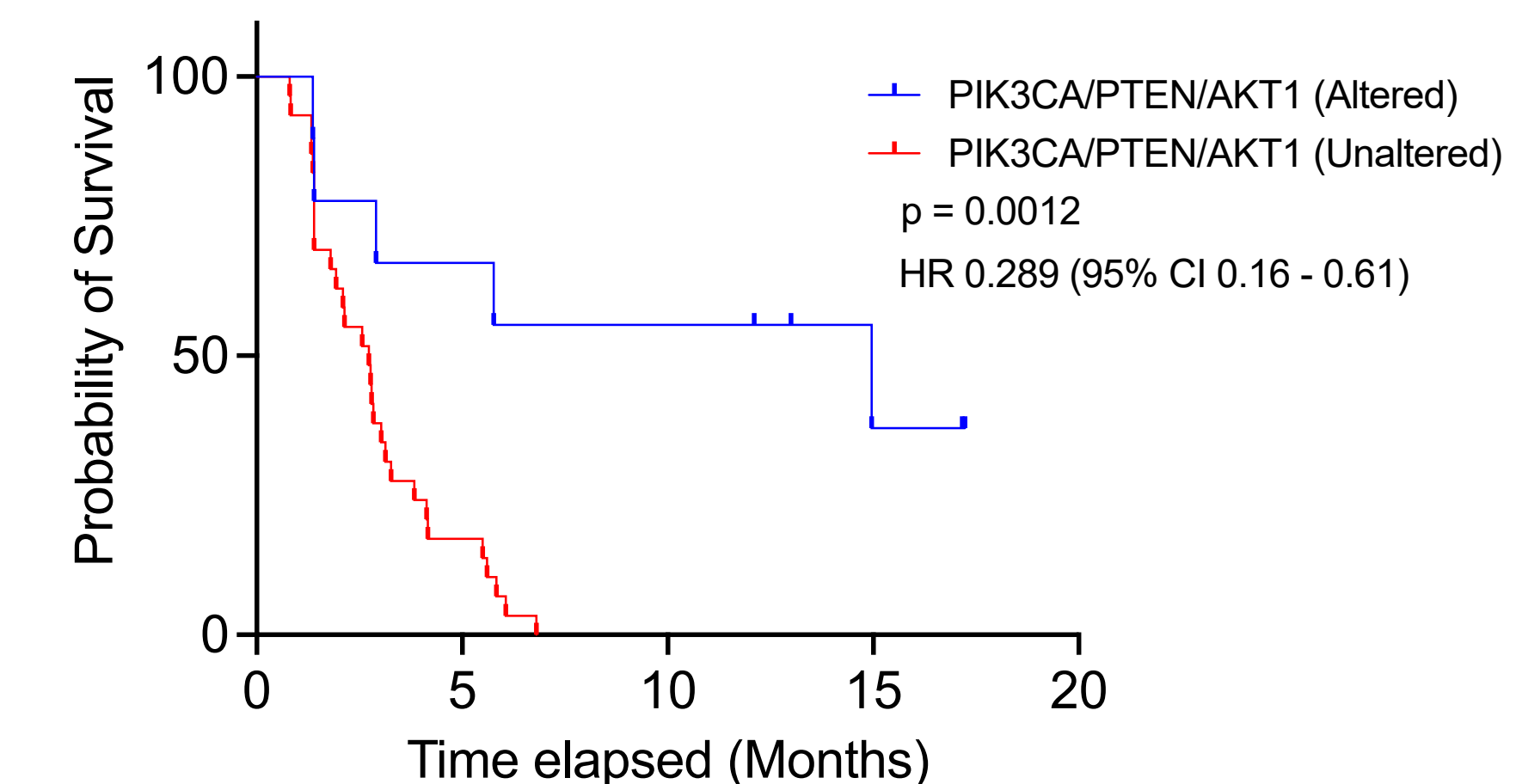


Patients with squamous histology demonstrated statistically significant improved PFS and a trend towards improved OS.

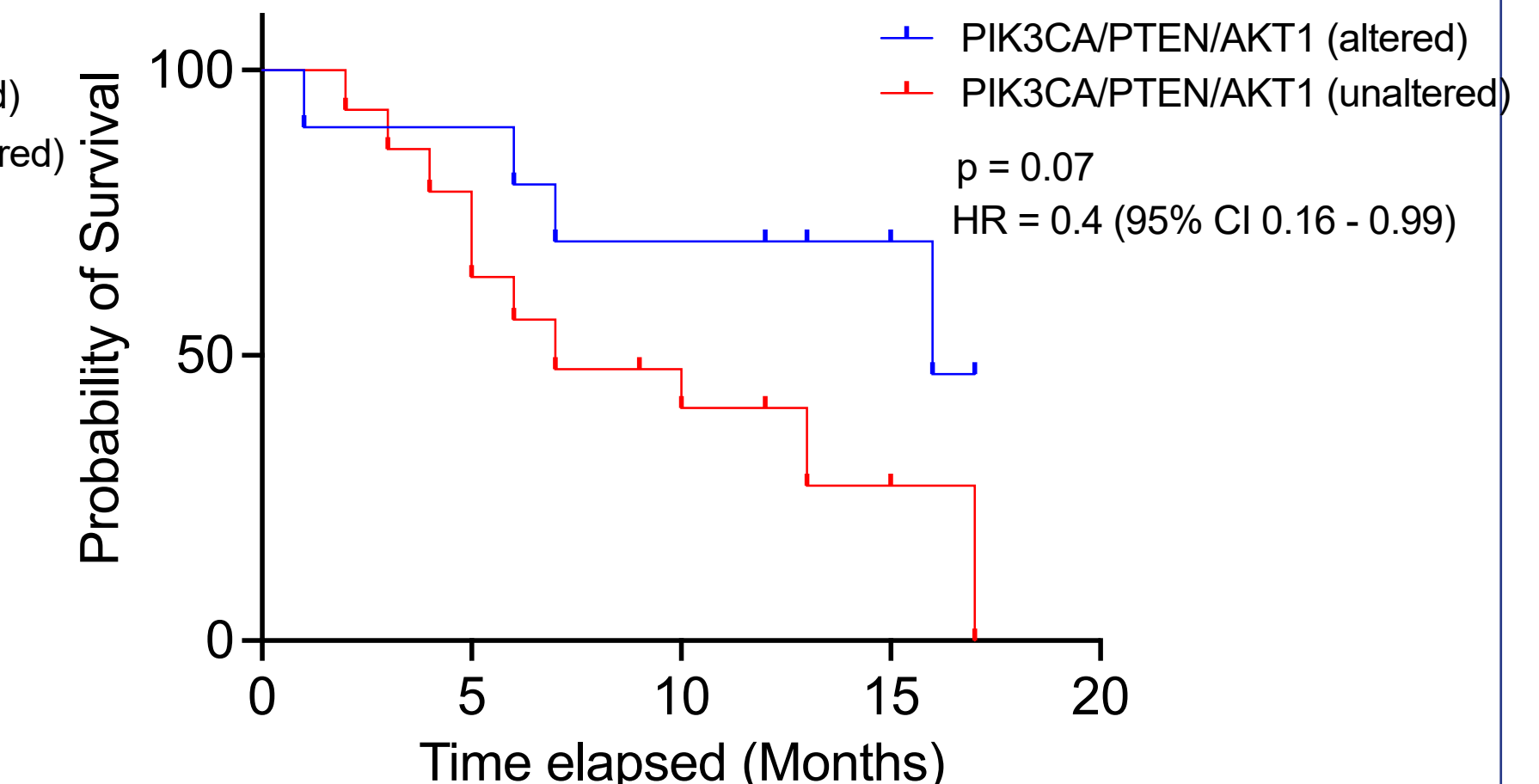


The presence of activating alterations in PIK3CA, AKT1 or PTEN predicted PFS (statistically significant) and OS (not statistically significant) benefit

PFS by Alteration Status



OS by Alteration Status



Demographics and Clinical Characteristic	
Characteristic	Population
Median age (range), yr	67.0 (49-91)
Sex — no. (%)	
Male	19 (47.5)
Female	21 (52.5)
Race or ethnic group	
White	27 (67.5)
Black	12 (30)
Other	1 (2.5)
Smoking history — no. (%)	
Never	4 (10)
Current	2 (5)
Former	28 (70)
Unknown	5 (12.5)
ECOG performance-status grade — no. (%)	
0	1 (2.5)
1	39 (97.5)

Histology	
Squamous	11 (27.5)
Nonsquamous	29 (72.5)
Metastatic disease stage, no. (%)	
No. of previous lines of therapy, no. (%)	
1	13 (32.5)
2	14 (35)
3	4 (10)
>3	7 (17.5)
Unknown	2 (5)
Median prior #of therapy (r 2.0 (1–5))	

DISCUSSION & FUTURE DIRECTION

- No unexpected adverse events.
- Final analysis of outcomes is pending data maturation.
- Further investigation in a larger confirmatory trial is planned to confirm the trends in squamous NSCLC.
- Translational pathway validation is ongoing.

REFERENCES

- Liu X, Bao X, Hu M, et al. Inhibition of PCSK9 potentiates immune checkpoint therapy for cancer. *Nature*. 2020;588(7839):693-698.

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