

A phase II study of AK112 (PD-1/VEGF Bispecific) in combination with chemotherapy in patients with advanced non-small cell lung cancer (NSCLC)

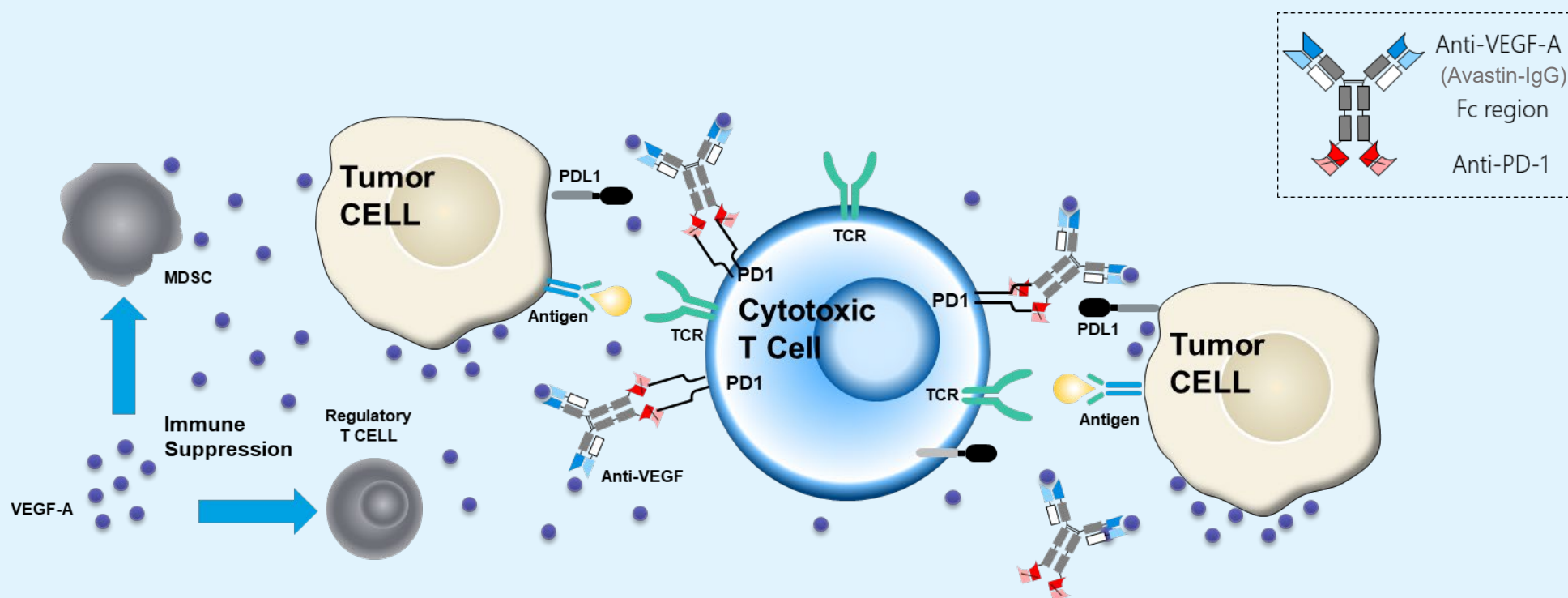
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Background

- AK112 is a humanized IgG1 bispecific antibody targeting PD-1 and VEGF (Figure 1).
- An early study showed AK112 with tolerable safety and promising anti-tumor efficacy in patients (pts) with advanced NSCLC (Refer to ASCO 2022 poster #9040). According to this study, AK112 20mg/kg Q3W was chosen as a recommended phase II dose (RP2D).
- Therefore, AK112 plus chemotherapy, is expected to further improve anti-tumor efficacy with favorable safety in 1L NSCLC (compared to anti-PD-(L)1 and chemotherapy combination therapies), EGFR+ advanced NSCLC, and IO-R NSCLC.
- Here, we present the recent results from a phase II study of AK112 plus chemotherapy in pts with advanced NSCLC.

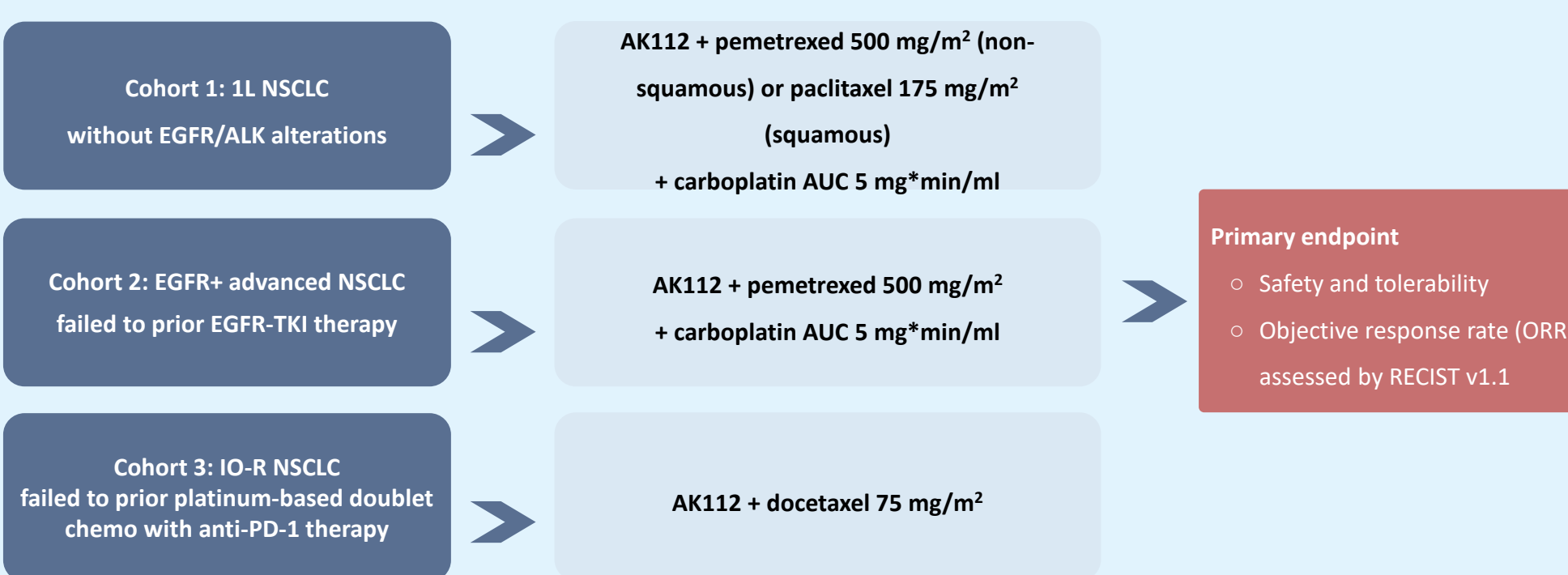
Figure 1. Schematic diagram of the mechanism of activity of AK112



Methods

- This was an open-label, multi-center phase II study evaluating the safety and efficacy of AK112 in combination with chemotherapy in pts with advanced NSCLC (NCT04736823).
- Enrolled pts were divided into 3 cohorts and treated with 10 or 20mg/kg AK112 plus chemotherapy once every 3 weeks (Figure 2).

Figure 2. Study design



Results

Patients

- 83 pts were enrolled from Feb 03, 2021 to Mar 20, 2022 to cohorts 1-3 and received at least one dose of AK112 plus chemotherapy. Baseline characteristics are shown in Table 1.
- Of 25 pts with squamous NSCLC, 52.0% were central type of squamous cell carcinoma and 28.0% had a history of hemoptysis.
- As of Mar 20, 2022, median duration of follow-up (95% CI) was 9.2 months (range: 7.7 - 9.7) for Cohort 1, 7.0 months (range: 5.6 - 7.1) for Cohort 2, and 5.9 months (range: 4.4 - 6.9) for Cohort 3.

Results (continued)

Table 1. Baseline Characteristics

Characteristics	Cohort 1 (N = 44)	Cohort 2 (N = 19)	Cohort 3 (N = 20)	Overall (N = 83)
Age, median (range), years	57.6 (44.3, 73.0)	60.2 (34.7 - 64.9)	60.0 (31.6 - 73.4)	58.03 (31.6 - 73.4)
Male, n(%)	28 (63.6)	6 (31.6)	16 (80.0)	50 (60.2)
ECOG performance status, n(%)				
1	42 (95.5)	14 (73.7)	19 (95.0)	75 (90.4)
Smoking status, n(%)				
Former or Current	24 (54.5)	4 (21.1)	15 (75.0)	43 (51.8)
Never	20 (45.5)	15 (78.9)	5 (25.0)	40 (48.2)
PD-L1 TPS, n(%)				
<1%	20 (45.5)	10 (52.6)	6 (30.0)	36 (43.4)
1-49%	16 (36.4)	6 (31.6)	8 (40.0)	30 (36.1)
≥50%	6 (13.6)	3 (15.8)	4 (20.0)	13 (15.7)
NE	2 (4.5)	0 (0.0)	2 (10.0)	4 (4.8)
Clinical Stage at Study Entry, n(%)				
IIIB/IIIC	4 (9.1)	0 (0.0)	3 (15.0)	7 (8.4)
IV	40 (90.9)	19 (100.0)	17 (85.0)	76 (91.6)
Histology, n(%)				
Squamous	18 (40.9)	0 (0.0)	7 (35.0)	25 (30.1)
Non-squamous	26 (59.1)	19 (100.0)	13 (65.0)	58 (69.9)
Brain metastasis, n(%)	8 (18.2)	7 (36.8)	1 (5.0)	16 (19.3)

Safety

- Treatment related adverse events (TRAEs) are summarized in Table 2.
- TRAEs leading to permanent discontinuation of AK112 occurred in 3.6% (3 pts).
- Most common TRAEs (≥10% of patients) included alanine/aspartate aminotransferase increased, anemia, amylase increased, white blood cell count decreased, neutrophil count decreased, epistaxis, and platelet count decreased.
- There was no significant difference in the incidences of TRAEs between the squamous and the non-squamous group.

Table 2. Overview of TRAE^[a]

Categories, n(%)	Overall (N = 83)	Squamous (N = 25)	Non-squamous (N = 58)
Any TRAE	71 (85.5)	20 (80.0)	51 (87.9)
Grade ^[b] 3-5 TRAE	20 (24.1)	8 (32.0)	12 (20.7)
Treatment Related SAE	15 (18.1)	7 (28.0)	8 (13.8)
TRAE leading to AK112 discontinuation	3 (3.6)	0 (0.0)	3 (5.2)
TRAE leading to death	1 (1.2)	0 (0.0)	1 (1.7)
Most common TRAEs (≥10% of patients)			
Alanine aminotransferase increased	17 (20.5)	5 (20.0)	12 (20.7)
Aspartate aminotransferase increased	15 (18.1)	3 (12.0)	12 (20.7)
Anemia	13 (15.7)	2 (8.0)	11 (19.0)
Amylase increased	12 (14.5)	2 (8.0)	10 (17.2)
White blood cell count decreased	12 (14.5)	4 (16.0)	8 (13.8)
Neutrophil count decreased	10 (12.0)	4 (16.0)	6 (10.3)
Epistaxis	10 (12.0)	4 (16.0)	6 (10.3)
Platelet count decreased	9 (10.8)	3 (12.0)	6 (10.3)
Haemorrhage related AESI			
Epistaxis	10 (12.0)	4 (16.0)	6 (10.3)
Hemoptysis	5 (6.0)	4 (16.0)	1 (1.7)
Haematuria	1 (1.2)	1 (4.0)	0 (0.0)
Haematochezia	1 (1.2)	1 (4.0)	0 (0.0)
Gingival bleeding	1 (1.2)	0 (0.0)	1 (1.7)
Anal haemorrhage	1 (1.2)	0 (0.0)	1 (1.7)
Conjunctival haemorrhage	1 (1.2)	0 (0.0)	1 (1.7)

[a] Treatment related indicates AK112 or AK112+chemo related; [b] Maximum reported CTCAE grade; SAE, serious adverse event; AESI, adverse event of special interest; CTCAE, common terminology criteria for adverse events.

- Haemorrhage related AESI included epistaxis, hemoptysis, haematuria, haematochezia, gingival bleeding, anal haemorrhage and conjunctival haemorrhage.
- Risk of haemorrhage correlated to anti-VEGF antibody declined significantly, even in pts with squamous NSCLC.

Efficacy

- In Cohort 1, of 43 evaluable pts, ORR and DCR were 77.8% (including 3 unconfirmed PR) and 100.0% for squamous NSCLC, 52.0% (including 1 unconfirmed PR) and 100.0% for non-squamous NSCLC, respectively (Table 3, Figure 3-A and B).
- In Cohort 2, of 19 evaluable pts, ORR and DCR were 68.4% and 94.7% (Table 3, Figure 3-C).
- In Cohort 3, of 20 evaluable pts, ORR and DCR were 40.0% and 80.0% (Table 3, Figure 3-D).

Table 3. Summary of Efficacy Outcomes

Response	Cohort 1		Cohort 2 (N = 19)	Cohort 3 (N = 20)
	Squamous (N = 18)	Non-squamous (N = 25)		
ORR, % (95% CI)	77.8 (52.4 - 93.6)	52.0 (31.3 - 72.2)	68.4 (43.4 - 87.4)	40.0 (19.1 - 63.9)
DCR, % (95% CI)	100.0 (81.5 - 100.0)	100.0 (86.3 - 100.0)	94.7 (74.0 - 99.9)	80.0 (56.3 - 94.3)

Figure 3. Waterfall plots and Spider plots

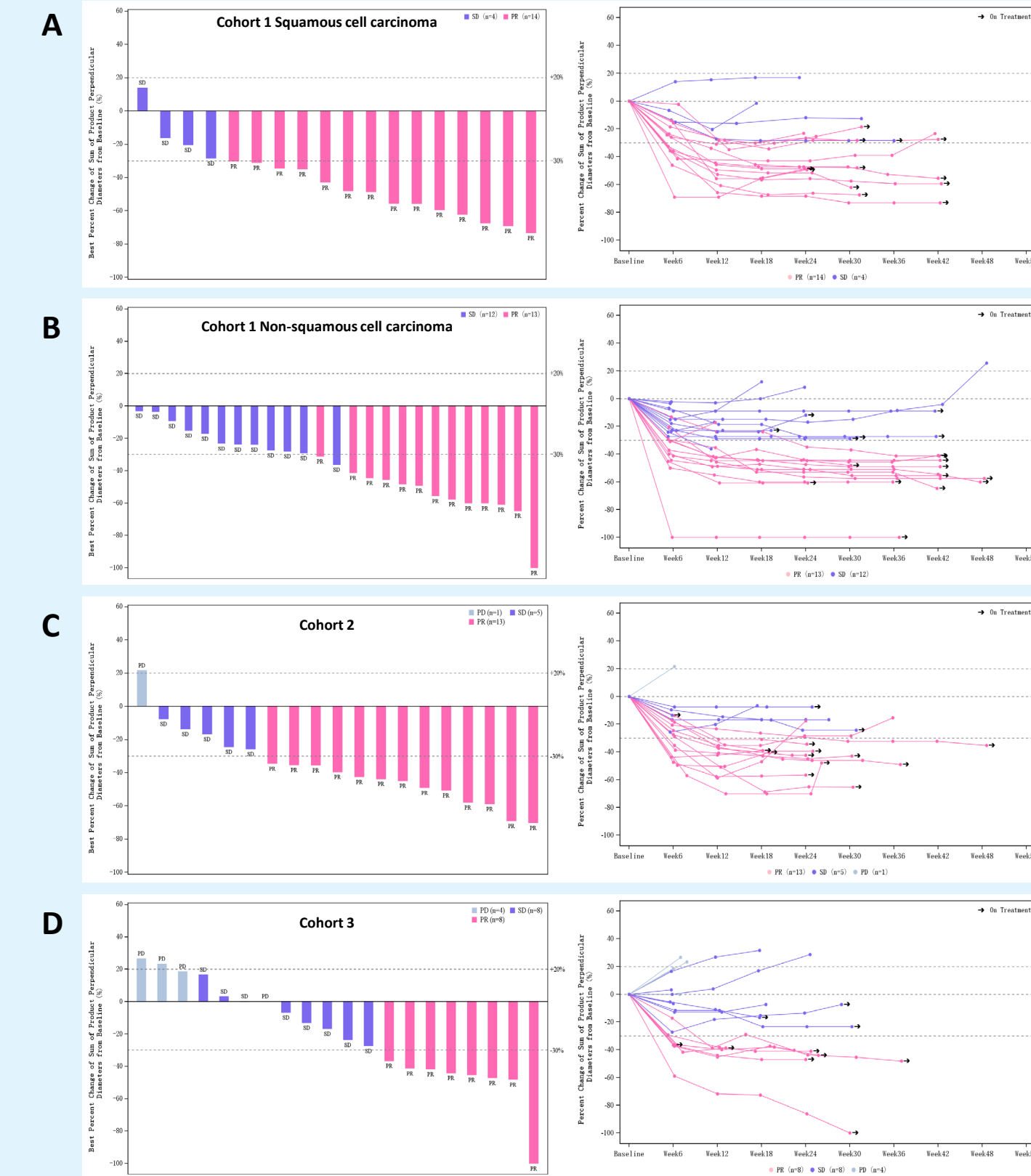
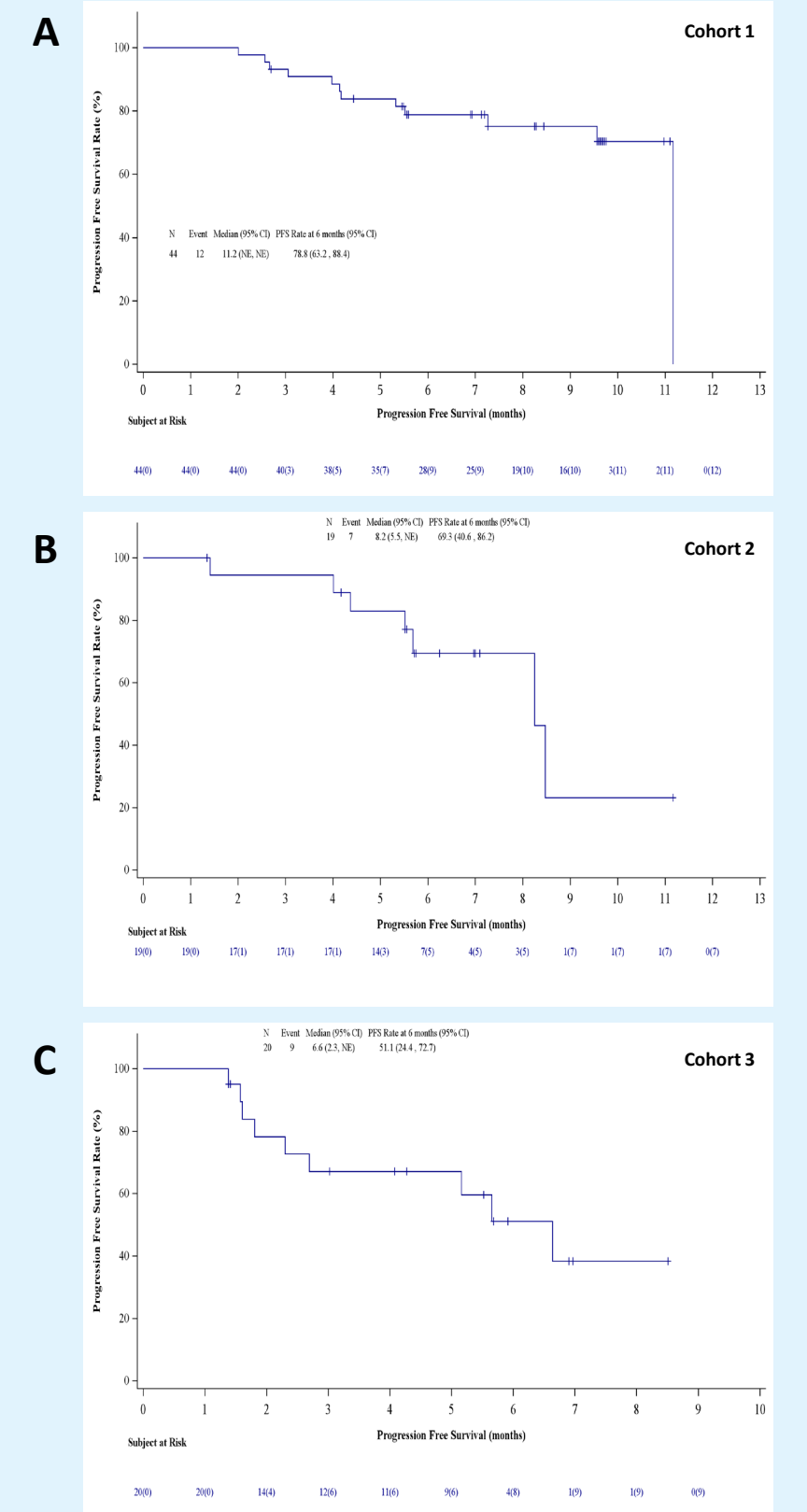


Figure 4. Kaplan-Meier Curves of PFS



- In Cohort 1, median PFS was not reached and 6-month PFS rate was 78.8% (95% CI: 63.2, 88.4) (Figure 4-A).
- In Cohort 2, median PFS was 8.2 months (95% CI: 5.5, NE) and 6-month PFS rate was 69.3% (95% CI: 40.6, 86.2) (Figure 4-B).
- In Cohort 3, median PFS was 6.6 months (95% CI: 2.3, NE) and 6-month PFS rate was 51.1% (95% CI: 24.4, 72.7) (Figure 4-C).

Conclusions

- AK112 in combination with chemotherapy demonstrated favorable safety characteristics and was well-tolerated, especially in pts with squamous NSCLC.
- In every cohort, AK112 plus chemotherapy demonstrated potentially superior anti-tumor activities.
- Therefore, a phase III study of AK112 plus chemotherapy versus chemotherapy in EGFR+ advanced non-squamous NSCLC failed to prior EGFR-TKI therapy (NCT05184712) is currently underway, and other phase III studies of AK112 plus chemotherapy in advanced NSCLC will be initiated soon.

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