The Frankfurt Institute of Clinical Cancer Research

Frankfurter Institut für Klinische Krebsforschung

IKF-s614: INSIGHT 003 evaluating feasibility of eftilagimod alpha (soluble LAG-3) combined with 1st line chemo-immunotherapy in metastatic non-small cell lung cancer (NSCLC) adenocarcinomas – a multicenter early phase trial –

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#1042P

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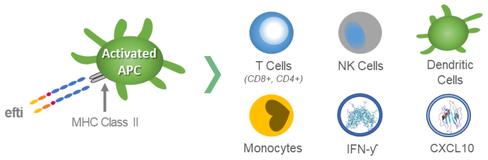
BACKGROUND

Stratum C of the INSIGHT multicenter platform trial evaluates eftilagimod alpha (efti) combined with standard of care (SOC) 1st line chemo-immunotherapy (IC) in metastatic non-squamous NSCLC patients (pts). Efti is an MHC class II agonist (soluble LAG-3 protein) activating antigen-presenting cells followed by T-cell (CD4/CD8) activation. Efti aims to enhance efficacy of IC. We hereby report the results from the first cohort of 21 pts.

Treatment of patients and collection of data is ongoing.

Figure 1: Mechanism of action of efti

Efti is soluble LAG-3 protein (LAG-3 domains fused to human IgG backbone). Activating Antigen Presenting Cells (APCs) with efti leads to a broader immune response, including increases in activated T cells (CD4/CD8) to fight cancer.

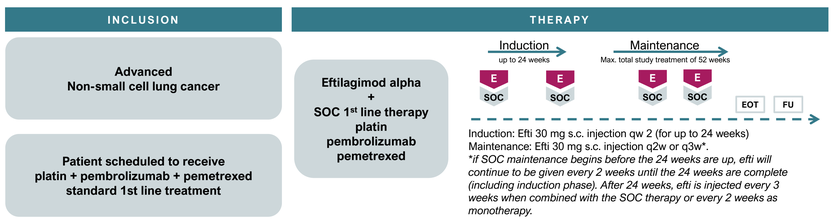


METHODS

Patients with 1st line advanced or metastatic NSCLC adenocarcinomas (non-squamous) receive carboplatin AUC5 / pemetrexed 500 mg/m² q3w 4 cycles followed by optional pemetrexed 500 mg/m² q3w maintenance plus pembrolizumab 200 mg q3w combined with s.c. efti (30 mg) (q2w for 24 weeks; thereafter q3w till week 52). Imaging: q8w. Primary endpoint: feasibility (safety / tolerability). Secondary endpoints include ORR*, PFS* and OS.

* Per RECIST 1.1.

Figure 2: Study Design



SUMMARY & CONCLUSION

Eftilagimod alpha combined with SOC in NSQ 1st line NSCLC (carboplatin/ pemetrexed/pembrolizumab) led to ORR >60%. For PD-L1 TPS <50% patient population, median PFS was 10.9 months and ORR 70.6%. Adding efti appears not to increase toxicity of the standard chemo-immunotherapy regimen. This combination appears to be feasible and safe, showing promising efficacy signals irrespective of PD-L1 expression status and especially in pts with TPS score < 50 %. Further evaluation of this regimen is strongly warranted (the cohort has been increased to 50 pts).

RESULTS

From August 2021 until April 2023, 21 patients were enrolled and received treatment.

Baseline Disease Characteristics:

- Median age: 65 years; 66.7% male; **Table 1.**
- Almost all (91 %) pts had metastatic disease at study entry and 81 % had a PD-L1 TPS < 50 %.

Efficacy:

- At data cut-off, unconfirmed ORR of 71.4% (confirmed ORR of 66.7%; **Table 2**).
- With a median follow up of 12.4 months, the ITT had a mPFS of 10.1 mo (**Table 2, Figure 3**) and mOS was not reached.
- Pts with negative or low PD-L1 status (TPS <50%) showed unconfirmed ORR of 70.6%, mPFS 10.9 mo and mOS not reached (**Table 4, Figure 4**).

Table 1: Baseline Characteristics

Baseline parameters		N=21
Age, median (range), years		65 (55-73)
Sex, n (%)	Female / Male	7 (33) / 14 (67)
ECOG PS score, n (%)	0 / 1	11 (52) / 10 (48)
Metastatic disease, n (%)	Yes / No	19 (91) / 2 (9)
PD-L1 expression TPS, n (%)	<1% 1-49% ≥50%	7 (33) 10 (48) 4 (19)

Table 2: Efficacy Overview

Best Overall Response (BOR) by RECIST 1.1	N=21 n (%)
Complete Response	0 (0.0)
Partial Response	15 (71.4)
Stable Disease	4 (19.0)
Progression	2 (9.5)
ORR confirmed, n (%)	**14 (66.7)**
ORR unconfirmed, n (%)	**15 (71.4)**
DCR, n (%)	19 (90.5)

PFS by RECIST 1.1 & OS	N=21
mOS ITT (% events)	NR (19.0)
12-mo OS rate, %	84.7
mPFS ITT (% events)	10.1 (52.4)
6-mo PFS rate, %	80.4
12-mo PFS rate, %	43.6

Safety & Exposure:

- Median number of administrations of therapy: efti: 16, Pembrolizumab: 12, Pemetrexed: 10, Platin: 4.
- No occurrence of unacceptable toxicities.
- 11 SAE (grade 1-2: 3; grade 3: 5; grade 4: 0; grade 5: 3) were reported (**Table 3**) in 7 pts (33 %).
- 1 pancreatitis and 1 allergic reaction were considered SUSARs.
- The most frequent AEs are listed in table 3.

Table 3: Summarized SAEs and AEs

Number of SAEs	N=11
Patients with ≥ 1 SAE	7
Patients with ≥ 1 SAE with relation to study treatment	3 (efti: 2)
SUSARs	Grade 3 Pancreatitis Grade 3 Allergic Reaction
Number of SAEs Grade ≥3	8
Listing of SAE terms	Dyspnea (18.2%) Bronchial infection (9.1%) Pancreatitis (9.1%) Sepsis (9.1%) Diarrhea (9.1%) SARS-COV-2 infection (9.1%) Mucositis oral (9.1%) Disease progression (9.1%) Lung infection (9.1%) Allergic reaction (9.1%)

Number of AEs	N=337
Patients with ≥ 1AE	21
Patients with ≥ 1 AE with relation to study treatment	20
Number of AEs Grade ≥3	101
Number of AEs related to efti	49
Most frequent AEs (incidence ≥10%)	Anemia (85.7%) Grade 1-2: 52.4% Grade 3: 33.3% Neutropenia (85.7%) Grade 2: 14.3% Grade 3-4: 71.5% Leukopenia (76.2%) Grade 1-2: 28.6% Grade 3-4: 47.6% Thrombocyopenia (66.7%) Grade 1-2: 42.8% Grade 3-4: 23.8% Fatigue (52.4%) Grade 1-2: 42.8% Grade 3: 9.5%

Figure 3: Progression-Free Survival

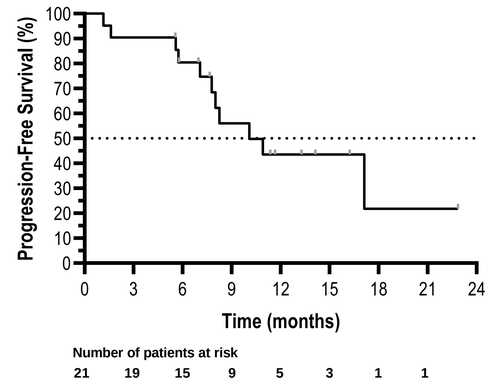
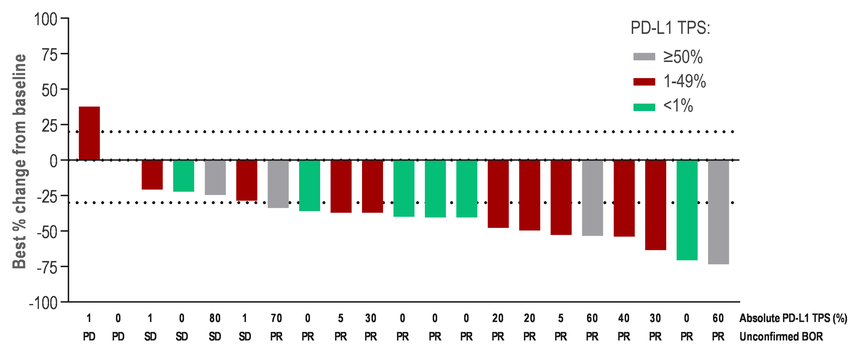


Table 4: Efficacy Overview by PD-L1 status

Tumor Response	PD-L1 expression level (TPS)			
	<1%, N=7	1-49%, N=10	≥50%, N=4	<50%, N=17
ORR* unconfirmed, n (%)	5 (71.4)	7 (70.0)	3 (75.0)	12 (70.6)
ORR* confirmed, n (%)	5 (71.4)	6 (60.0)	3 (75.0)	11 (64.7)
mPFS*, months (% events)	10.1 (42.9)	10.9 (60.0)	7.1 (50.0)	10.9 (52.9)
mOS, months (% events)	17.4 (28.6)	NR (10)	NR (25)	NR (17.6)

* Per RECIST 1.1.

Figure 4: Best Overall Response from Baseline by PD-L1 status



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Disclosures

TOG: no conflict of interest.
AA: no conflict of interest.

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