Impact of high fasting plasma glucose in the clinical outcome of patients with advanced NSCLC with PD-L1 ≥ 50% treated with frontline pembrolizumab (1315P)

S. Llop[1], E. Puig[2], R. Palmero[1], J. Brenes[1], N. Vilariño[1], J.C. Ruffinelli[1], C. Mesía[1], J.Saldaña[1], M. Jové[1], I.Brao[3], M.Arellano[3], F. Luciano-Mateo[4], I. Peiró[5], C. Muñoz-Pinedo[4], E. Nadal[1]

1.Medical Oncology, Institut Català d'Oncologia, l'Hospitalet de Llobregat, Spain; 2. Medical student, Barcelona University, Bellvitge; 3. Lung Functional Unit, Institut Català d'Oncologia, l'Hospitalet de Llobregat, Spain; 4. Metabolism and Cell Death group, Oncobell, IDIBELL. 5. Functional Nutrition Unit, Institut Català d'Oncologia, l'Hospitalet de Llobregat, Spain

BACKGROUND

- Hyperglycemia is associated with poor outcome in patients (pts) with curable non-small cell lung cancer (NSCLC), but its role in pts with advanced NSCLC is unknown.
- Single-agent pembrolizumab is the standard first-line treatment for NSCLC patients (pts) with high PD-L1 expression (≥ 50%).
- About a third of pts will experience early progression to pembrolizumab and markers predicting unfavorable outcome are urgently needed.
- **This retrospective study aims to evaluate factors predicting response, progression free survival and overall survival in pts with advanced NSCLC with high expression of PD-L1 who received Pembrolizumab as first line therapy.**

METHODS

- Retrospective study to assess the prognostic value of high fasting plasma glucose (HFG, >7 mmol/L) in a cohort of stage IV EGFR/ALK negative NSCLC pts with PDL1 ≥ 50% who received frontline pembrolizumab.
- The study was approved by the local Ethics Committee.
- Demographic and laboratory data, ECOG performance status (PS) and clinical outcome data were collected.
- Progression-free survival (PFS) and overall survival (OS) were estimated by Kaplan–Meier method.
- A multivariate Cox regression model and log-rank test were performed.

First author has no conflicts of interest to declare

RESULTS

Patients' characteristics

- From August 2017 to June 2020 66 pts were included in this study. Median age was 64.6 years old (40-90); 50 pts (75.8%) were males and 10 (15.2%) and most patients were smokers (90.9%) and had adenocarcinoma (66.6%). Ten pts (15.2%) presented liver metastases (mets) at diagnosis.
- HFG was found in 20 pts (30.3%) at diagnosis, being only 45.0% of them previously diagnosed with type 2 diabetes.
- No differences were found according to gender, smoking history, comorbidities, PS, tumor histology or PDL-1 expression between HFG and non-HFG groups.

Table 1. Baseline characteristics

	HFG (n = 20)	Non – HFG (n = 46)	P-value
Age, Median [range]	64.1 [49-77]	65.0 (40-90)	0.747*
Sex, n (%)			
Male	16 (80.0%)	34 (73.9%)	0.758**
Female	4 (20.0%)	12 (6.1%)	
Smoking status, n (%)			
Non – smoker	2 (10.0%)	4 (8.7%)	0.684***
Former smoker	9 (45.0%)	26 (56.5%)	
Current smoker	9 (45.0%)	16 (34.8%)	
Comorbidities, n (%)			
Respiratory disease	5 (25.0%)	6 (13.0%)	0.287**
Hypertension	13 (65.0%%)	22 (47.8%)	0.284**
Cardiovascular disease	7 (35.0%)	13 (28.3%)	0.576**
Diabetes Mellitus	9 (45.0%)	6 (13.0%)	**0.009****
Histology, n (%)			
Adenocarcinoma	11 (55.0%)	33 (71.7%)	0.373***
Squamous cell carcinoma	5 (25.0%)	6 (13.0%)	
Other	4 (20.0%)	7 (15.2%)	
PS at diagnosis, n (%)			
0	2 (10.0%)	8 (17.4%)	0.114***
1	15 (75.0%)	37 (80.4%)	
2	3 (15.0%)	1 (2.2%)	
PD-L1 status, n (%)			
50 – 79	14 (70.0%)	28 (60.9%)	0.583**
80 - 100	6 (30.0%)	18 (39.1%)	

*Student's t-Test; **Fisher's test; ***Chi-squared test

Survival analysis

- With a median follow up of 18 months (m), HFG was significantly associated with liver mets (p=0.001) and early progression at 3 months (p=0.003).

Fig 1. Glycemia level according to liver mets.

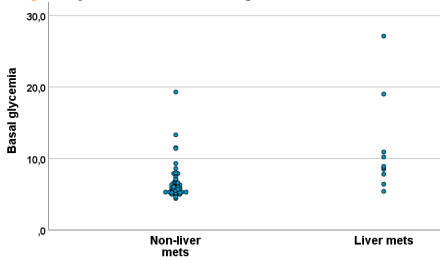
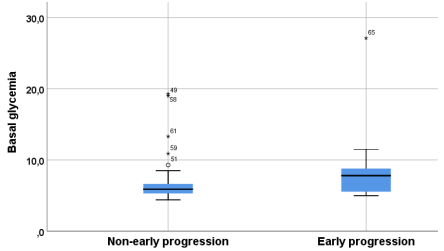


Fig 2. Glycemia level according to early progression.



- Median PFS was significantly shorter in pts with HFG (2.2 m; 95% CI 1.9-2.5 m) vs non-HFG (27.0 m; 95% CI 11.2-42.8; p=0.001). Median OS was significantly shorter in pts with HFG (6.0 m; IC95% 0.0-13.5 m) vs non-HFG (40.7 m; 95% CI 22.6-58.9; p=0.002).

Fig 3. PFS according to HFG (HFG 2.2 m vs non-HFG 27.0 m)

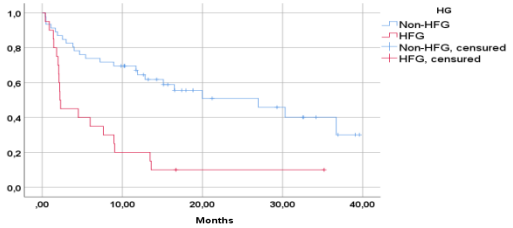
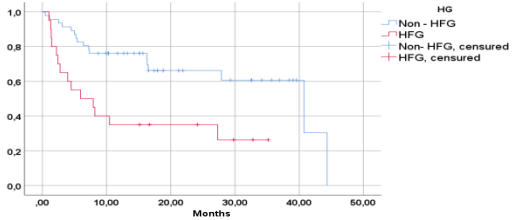


Fig 4. OS according to HFG (HFG 6.0 m vs non-HFG 40.7m)



- In the univariate analysis, HFG, ECOG PS and liver mets at diagnosis were significantly associated with worse PFS. In the multivariate analysis for PFS, HFG remained as independent prognostic factor (HR 2.73; 95% CI 1.34-5.56, p=0.006), after adjusting by ECOG PS and presence of liver mets.

CONCLUSIONS

- Baseline HFG is independently associated with worse PFS and early tumor progression at 3 months in this cohort of pts treated with frontline pembrolizumab
- Prospective studies in larger cohorts of NSCLC pts treated with immunotherapy are warranted to confirm this association

slloperna@gmail.com; esnadal@iconcologia.net