15th MADRID CONGRESS on Lung CANCER

23&24 November 2023

#15CongressGECP

Fundación GECP lung cancer research

Unveiling the Immune Key: HLA-I and CD73 as a Catalyst for Long-Term Triumph in Non-Small Cell Lung Cancer Patients Undergoing Immunotherapy

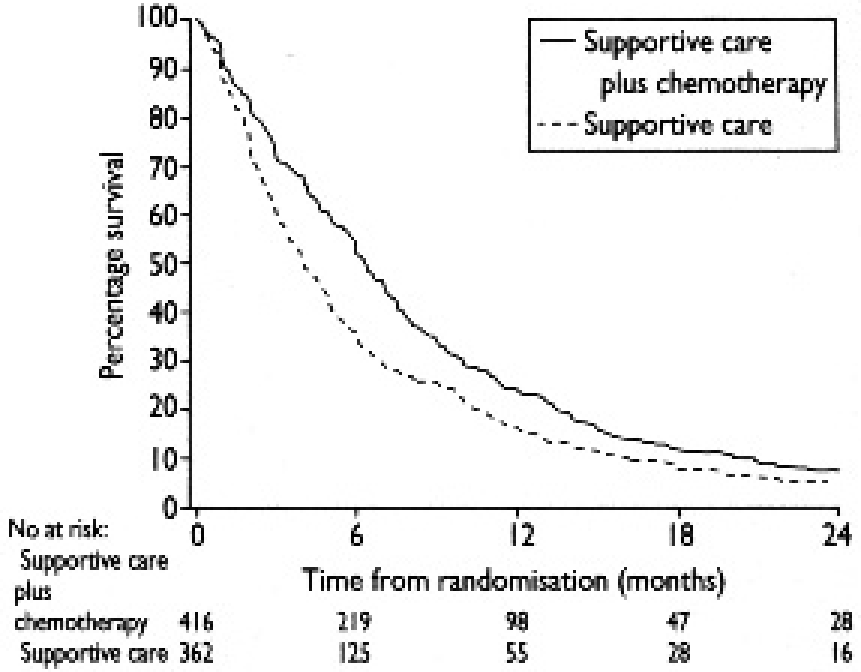
Enric Carcereny[1,5], Maria Saigí[1,5], Anna Esteve[1,3], Jose Luís Mate[2], Marta Domènech[1,5], Felipe Andreo[4], Gabriela Cerdá[1], Ainhoa Hernández[1,5], Anna Martinez- Cardús[5], Marc Cucurull[1,5], Carmen Centeno[4], Eva Pros[6], Assumpció Lopez-Paradís[1], Teresa Morán[1,5], Alba Hernández-Gallego[2], Montse Sánchez Céspedes[6]

Medical Oncology Department, Catalan Institute of Oncology (ICO)-Badalona, Germans Trias i Pujol Research Institute (IGTP); Badalona, Barcelona, Spain.[1]Pathology Department, Germans Trias i Pujol University Hospital (HUGTiP), Germans Trias i Pujol Research Institute (IGTP); Badalona, Barcelona, Spain.[2] Research Unit, Catalan Institute of Oncology (ICO)-Badalona, Barcelona, Spain [3]·Pneumology Department, Germans Trias i Pujol University Hospital (HUGTiP), Germans Trias i Pujol Research Institute (IGTP); Badalona, Barcelona, Spain.[4]Badalona·Applied Research Group in Oncology (B·ARGO), Germans Trias i Pujol Research Institute (IGTP); Badalona, Barcelona, Spain.[5]Cancer Genetics Group, Josep Carreras Leukaemia Research Institute (IJC), Badalona, Barcelona, Spain.[6]

Background

LONG TERM RESPONDERS or LONG TERM SURVIVORS

- Several studies have established the definition of long-term survival in advanced NSCLC at more than 2 years from the time of diagnosis



Okamoto T et al. Lung Cancer 2005 Satoh H Anticancer Res 2007 Dujon C et al. Rev Mal Respir 2009 Giroux Leprieur E et al Respirology 2012 Van Damme V et al Lung Cancer 2013

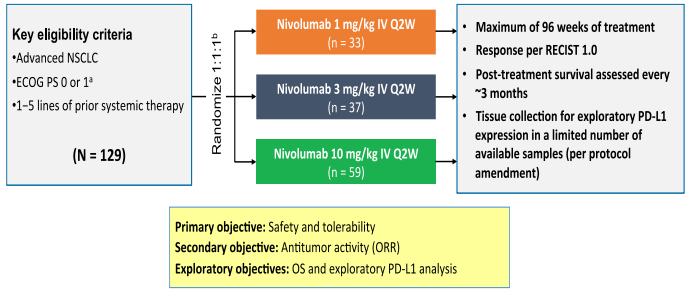
Carbone et al BMJ 1995

Background

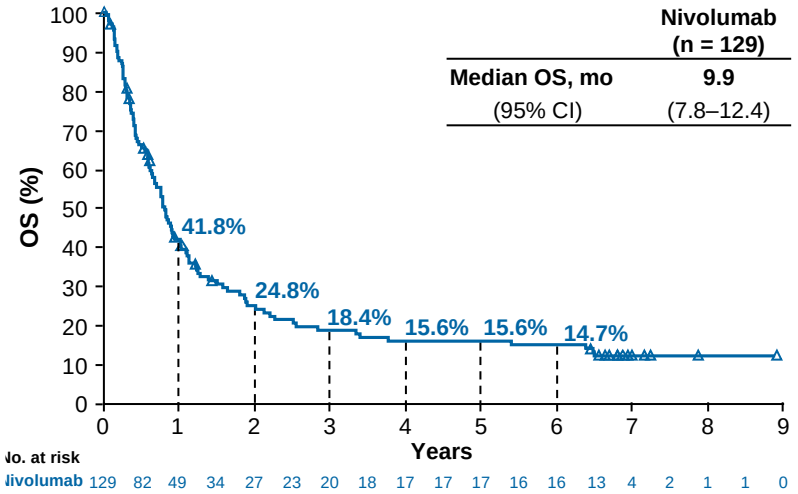
LONG TERM RESPONDERS or LONG TERM SURVIVORS

CA209-003

Phase 1 Study of Nivolumab in Advanced Solid Tumors (NSCLC Cohorts)



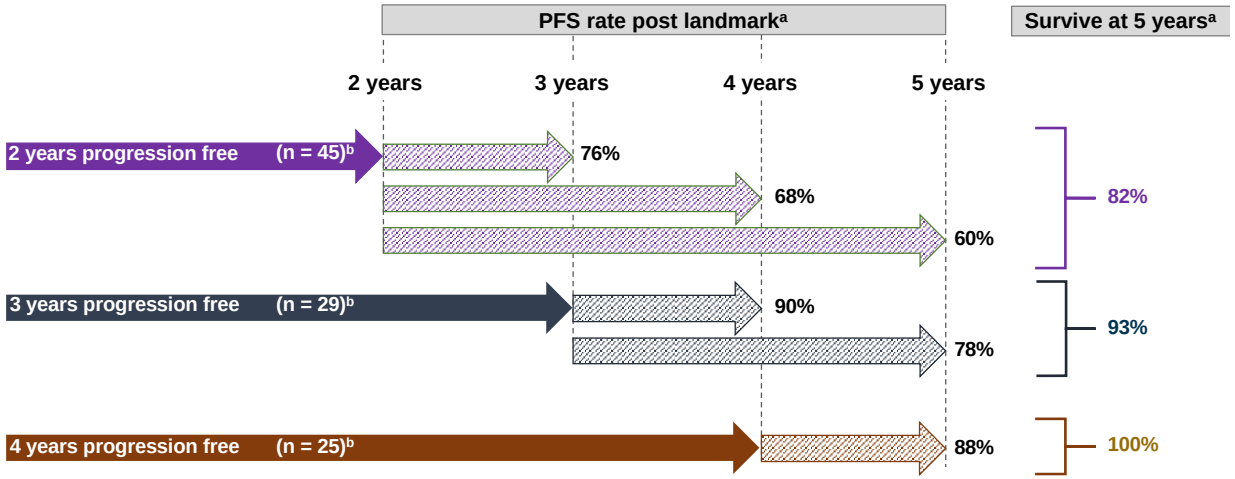
- Primary safety/efficacy and 3-year follow-up data have been published previously[1,2]
- **Minimum follow-up for the present analysis was 58.25 months (15-Nov-2016 database lock)**



	Nivolumab (n = 129)
Median OS, mo	**9.9**
(95% CI)	(7.8–12.4)

Bhramer J el al ACCR 2017

CheckMate 017 and 057: PFS and OS Landmark Analyses by PFS at 2, 3, and 4 Years

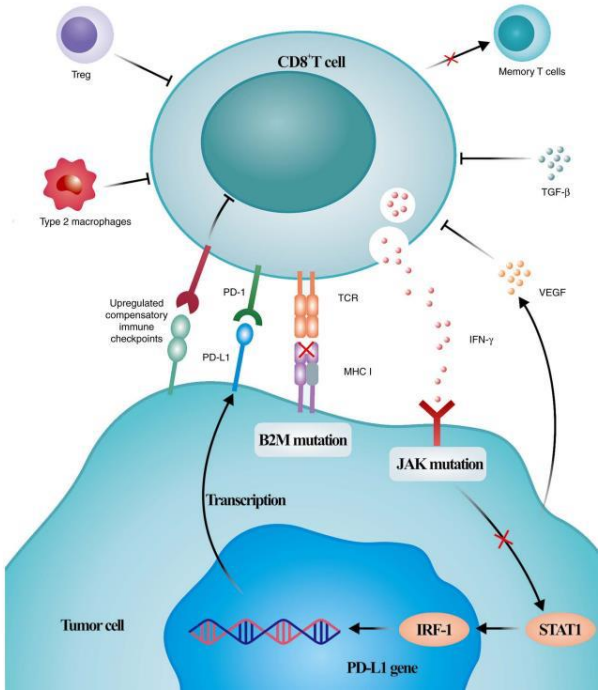


[a]Based on Kaplan–Meier estimates; [b]Number of patients at risk.

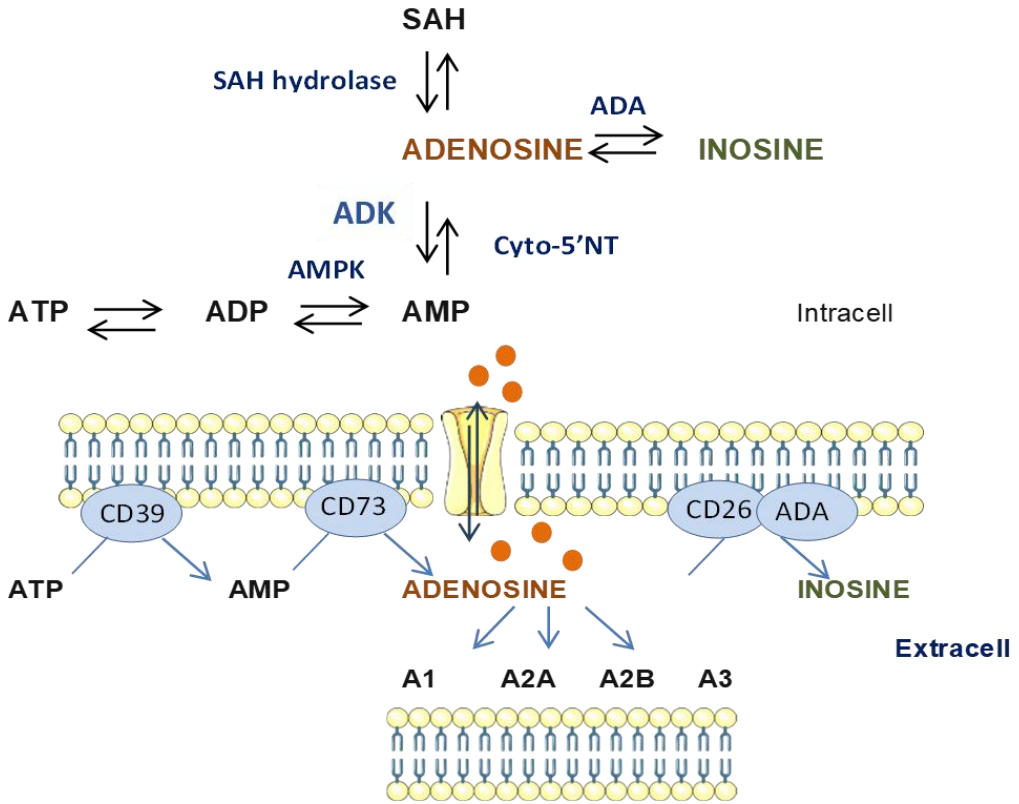
Background

HLA and CD73

HLA-I is essential for antigen presentation



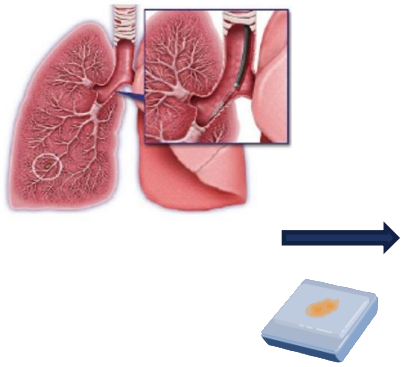
Zaretsky JM, NEJM 2016
Pereira C Clin Can Res 2017
Mahadevan NR Cancer Discov 2021
Xiaoran MA, Int journ Oncol 2022



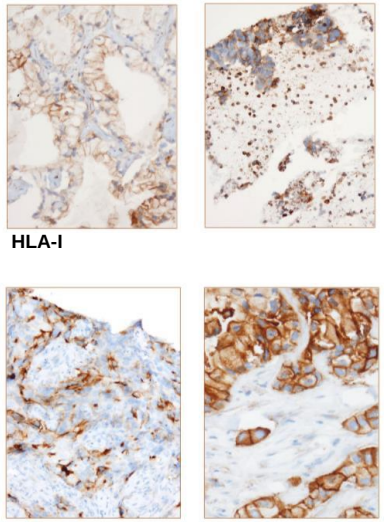
Adapted from Passarelli et al. 2019

Methods

N=145 metastatic NSCLC patients treated with immunotherapy (IT) based therapy between 2014 and 2019 at ICO Badalona (IRB PI-19-275)



FFPE human tissue



HLA-I

CD73

IHC	Clone	Tested	Excluded*	Total
PD-L1	Ventana SP 263	113	32	145
HLA-I	Abcam EMR 8-5	88	57	145
CD73	Cell Signaling D7F9A	84	61	145

- To identify Long-Term Responders (LTR), we investigated the influence of progression-free status on extended survival. An exploratory landmark analysis was carried out to determine the 5-year Overall Survival (OS) rates based on progression-free status concerning ICIs at the 6, 12, and 24-month marks.
- We examined the levels of expression, using immunohistochemistry, of HLA-I and other immune-related markers, including CD73, CD8+ tumor-infiltrating lymphocytes (TILs), and PD-L1 (Ventana SP263), using formalin-fixed paraffin-embedded human tissue samples.
- Our evaluation included an assessment of responses and clinical outcomes linked to ICIs.
- We employed the Chi-Square test for categorical variables and the Kaplan-Meier method for survival analysis. Significance was determined with a threshold of $p < 0.05$.

Results

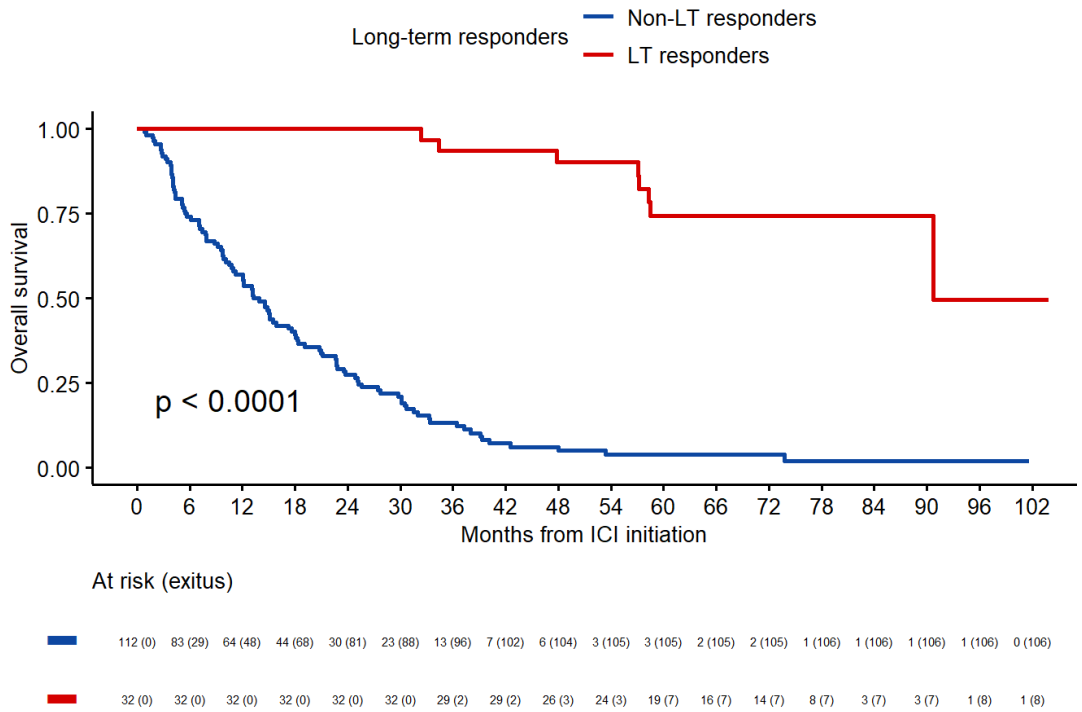
Clinical and molecular characteristics of non-LTR and LTR NSCLC patients.

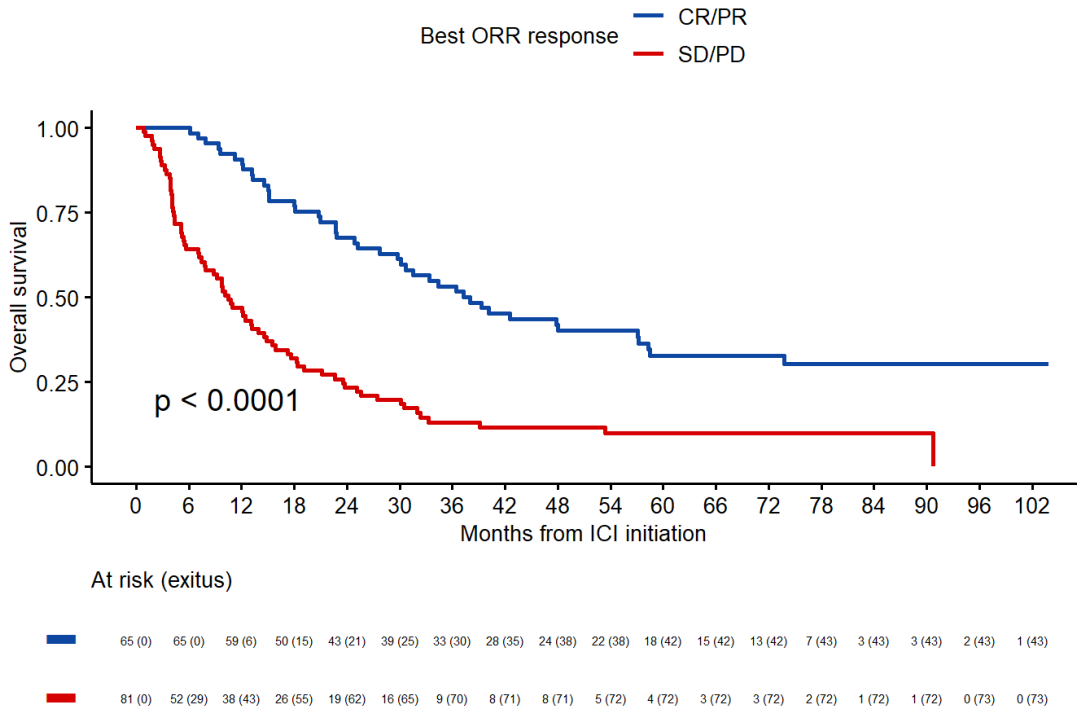
Characteristic	Non-LTRs n=114	LTRs n=32	*P*
Age at diagnosis (y) Median [IQR]	65 [58-71]	59 [53-63]	0.011
Gender, n (%)			1
Female	15 (13.1%)	4 (12.5%)	
Male	99 (86.8%)	28 (87.5%)	
Smoking status, n (%)			0.286
Current	60 (53.6%)	21 (70%)	
Former	42 (37.5%)	7 (23.3%)	
Never	10 (8.9%)	2 (6.7%)	
Pack/y, Median [IQR]	50 [37-70]	45 [32-60]	0.312
Histopathology, n (%)			0.767
LuADs	68 (59.6%)	22 (68.8%)	
LuSCCs	40 (35.1%)	7 (23.3%)	
NSCLC-NOS	6 (5.2%)	1 (3.1%)	
ECOG, n (%)			0.262
0	26 (23.4%)	11 (35.5%)	
1	85 (76.6%)	20 (64.5%)	
Disease Stage at baseline, n (%)			0.435
I/II	12 (9.9%)	2 (6.2%)	
III	27 (27.7%)	12 (37.5%)	
IV	70 (64.2%)	18 (56.2%)	

	Non-LTRs	LTRs	
Schedule received, n (%)			0.721
ICI	95(83%)	26 (81%)	
ICI-ICI	11 (10%)	3 (9.5%)	
ChT-ICI	8 (7%)	3 (9.5%)	
Line of ICI treatment, n (%)			0.312
1st L	34 (29.8%)	9 (28.1%)	
2nd L	55 (48.2%)	12 (37.5%)	
3rd L	25 (21.9%)	11 (34.4%)	
Best ORR response, n (%)			**<0.001**
Complete Response (CR)	2 (1.7%)	8 (25%)	
Partial Response (PR)	39 (34.2%)	16 (50%)	
Stable Disease (SD)	43 (37.7%)	7 (21.9%)	
KRAS, n (%)			1
KRAS mutant	22 (39.3%)	8 (40%)	
KRAS wild type	34 (60.7%)	12 (60%)	
HLA-I, n (%)			**0.011**
Low	45 (66.1%)	7 (33.3%)	
High	23 (33.8%)	14 (66.6%)	
PD-L1, n (%)			0.463
Low	65 (76.4%)	20 (68.9%)	
High	20 (23.5%)	9 (31.0%)	
CD73, n (%)			0.103
Low	52 (55.9%)	14 (48.3%)	
High	10 (10.8%)	8 (27.6%)	

Results

Overall survival by LTR and respose to ICI

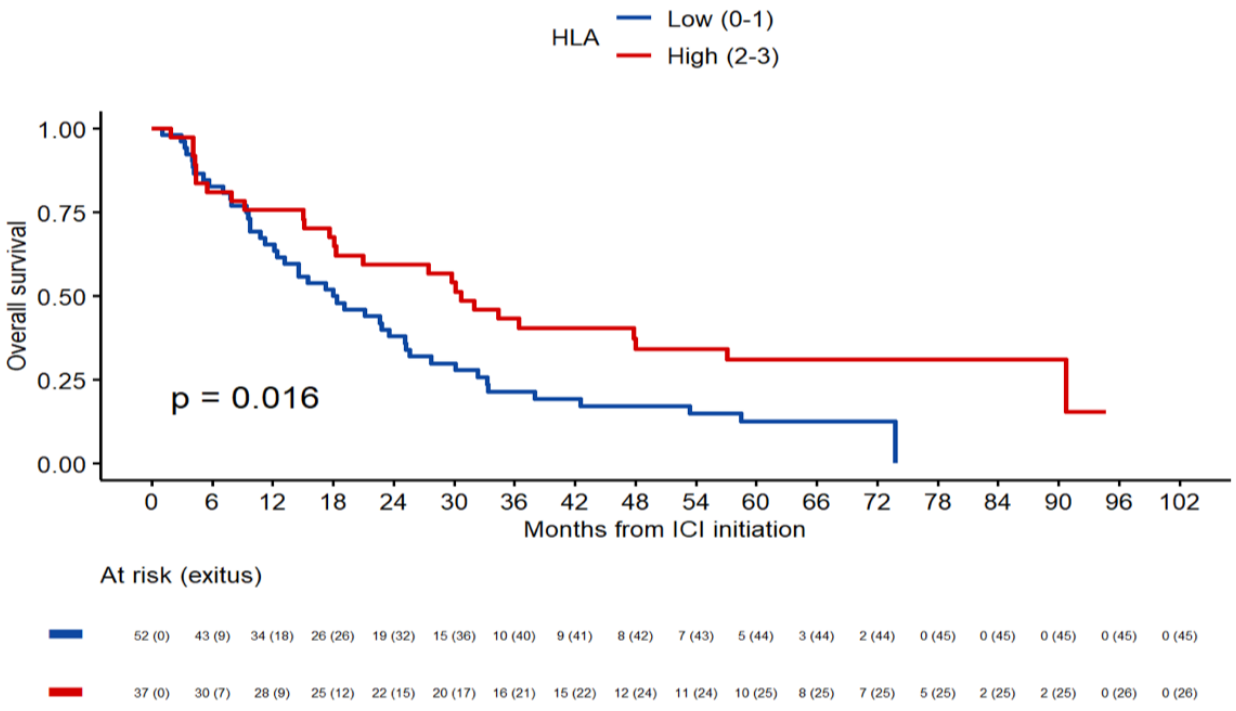




Results

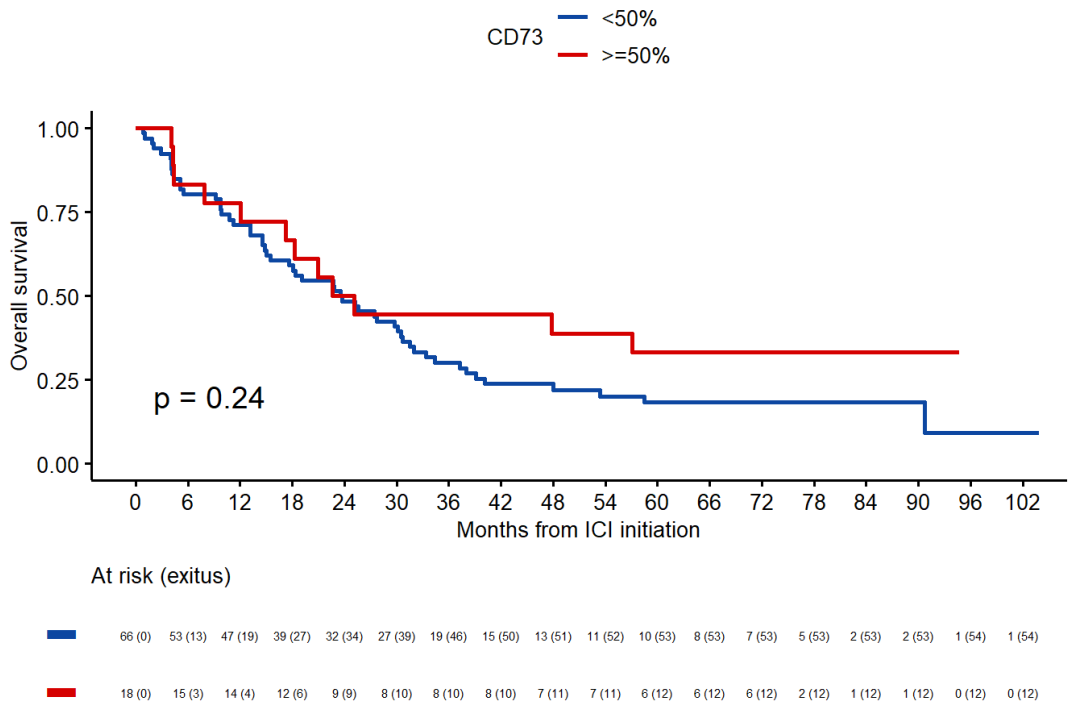
Overall Survival by HLA and CD73

HLA



LTR patients had higher HLA-I expression (68%) than non-LTR (35%) (p= 0.013).

CD73



Median CD73 expression was higher in LTR: 35% (95% CI 10-57.5) than non-LTR: 5% (95% CI 0-23.8) p=0.007.

Conclusions

The identification and development of predictive biomarkers for long-term benefit with ICIs is required.

In our cohort, we characterized a subset of LTR to ICIs (22% of patients).

This subgroup of patients was enriched with HLA-I expression and higher levels of CD73, which are emerging immunocheckpoints in NSCLC and predictors of LTR to ICIs.

Aknowledgements

IMMUNOLUNG PROJECT

Salut/ ICO Institut Català d'Oncologia
IGTP Germans Trias i Pujol Research Institute
Germans Trias i Pujol Hospital
Josep Carreras LEUKAEMIA Research Institute
B·ARGO Badalona - Applied Research Group in Oncology


15th
MADRID
CONGRESS
on Lung CANCER
23&24
November 2023
#15CongressGECP
Fundación
GECP
lung cancer
research
Muchas Gracias