Iniciativa científica de:

GECP lung cancer research

LUNG CANCER UPDATES

ASCO HIGHLIGHTS

31 MAYO - 4 JUNIO 2019

Con la colaboración de:

Bristol-Myers Squibb

illumina

Lilly

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Inmunoterapia en pacientes VIH positivos

Dra. Ana Laura Ortega

Día 2

Con la colaboración de:

Bristol-Myers Squibb
illumina
Lilly

Phase 1 study of pembrolizumab in people with HIV and cancer

2019 American Society of Clinical Oncology Annual Meeting
June 2, 2019
Chicago, IL

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Fred Hutchinson Cancer Research Center

cancer immunotherapy trials network

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NIH NATIONAL CANCER INSTITUTE Center for Cancer Research

Inmunoterapia en VIH: fase 1 pembro

Cancer Immunotherapy Trials Network-12

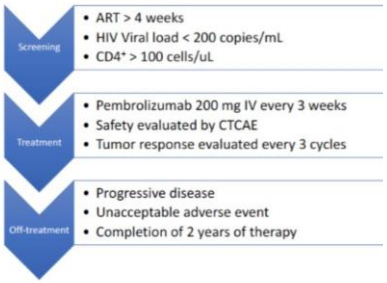
Study Design

- Multicenter phase I study

Primary Objective

- Evaluate safety in 3 cohorts:
  - Cohort 1: 100-199 CD4⁺ T cells/μL
  - Cohort 2: 200-350 CD4⁺ T cells/μL
  - Cohort 3: >350 CD4⁺ T cells/μL

Study Schema



Cancers

Cancer	All	Cohort 1 CD4⁺ 100-199 cells/μL	Cohort 2 CD4⁺ 200-350 cells/μL	Cohort 3 CD4⁺ >350 cells/μL
AIDS Defining	11			
Kaposi sarcoma	6		2	4
Primary Effusion Lymphoma	2	1	1	
Diffuse Large B-cell Lymphoma	3		1	2
Non-AIDS Defining	19			
Anal Cancer	6	4	2	
Tonsillar cancer	1			
Metastatic skin, squamous cell cancer	3	1	1	1
Non-Small Cell Lung Cancer	1		1	
Hepatocellular Carcinoma	1		1	
Sarcomatoid Lung Cancer	1			1
Bladder Cancer	2			2
Pancreatic Cancer	1			1
Cholangiocarcinoma	1		1	
Prostate cancer	1		1	
Adenoid cystic carcinoma	1			1

Immune Related Events of Clinical Interest

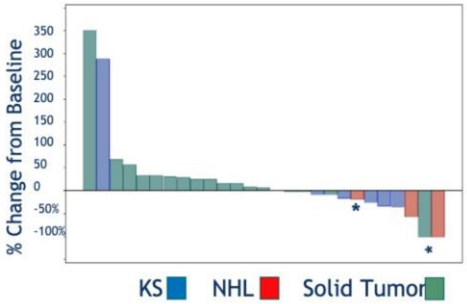
- Immune related adverse events of clinical interest ≥ grade 2
- Management
  - Holding pembrolizumab and administering steroids
  - Hypothyroidism: levothyroxine and continued pembrolizumab

Immune Related Events of Clinical Interest	
Adverse Event	n
Hypothyroidism	6
Pneumonitis	3
Rash	2
LFT abnormalities	1
Musculoskeletal	1
KSHV-lymphoproliferative disorder	1

Best Overall Response

Best Response	n
Complete	**1 (Lung)**
Partial	**2 (NHL)**
Stable >24 week	**2 (KS)**
* Lugano Immune Response 3	2
Stable <24 week	13
Progressive Disease	8
Not evaluable	1

Waterfall Plot



PRESENTED AT: 2019 ASCO ANNUAL MEETING #ASCO19 PRESENTED BY:

Inmunoterapia en VIH: DURVAST

Abs 2501

Phase II study of durvalumab (MEDI4736) in HIV-1-infected cancer patients

M. Gonzalez-Cao[1], T. Moran[2], J. Dalmau[3], J. Garcia-Corbacho[4], R. Bernabe[5], O. Juan[6], J. de Castro[7], R. Blanco[8], A. Meyerhans[9,10], J. Blanco[3,11], J. Prado[3], N. Karachaliou[1], C. Brander[3,10-11], J. Carrillo[3], B. Clotet[2,3,11], B. Massuti[12], M. Provencio[13], MA. Molina[1], J. Martinez-Picado[3,10-11], R. Rosell[1,14] on behalf of the Spanish Lung Cancer Group.

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GECP lung cancer research

Inmunoterapia en VIH: DURVAST

Study Objectives and Design: DURVAST (NCT 03094286)

1. **Primary endpoint:** Feasibility /Safety

2. **Secondary endpoint:** ORR (RECIST v1.1), PFS, OS

Inclusion Criteria
-HIV-1 infection
-Advanced cancer
-Naive or pretreated patients
- Effective ART

Exclusion Criteria
-Previous treatment with anti PD-1/PD-L1 antibodies
-Co-infections (TB, HBV, HCV)

N 20 → **Durvalumab iv 1500 mg Q 4w** → Follow-up Treatment until PD* or toxicity
*Treatment continuation was allowed in case of PD with clinical benefit

3. **Exploratory endpoints:**
3.1. HIV reservoir, virus replication, composition of circulating T cells
3.2. Molecular predictive factors of antitumoral activity/safety

Baseline characteristics

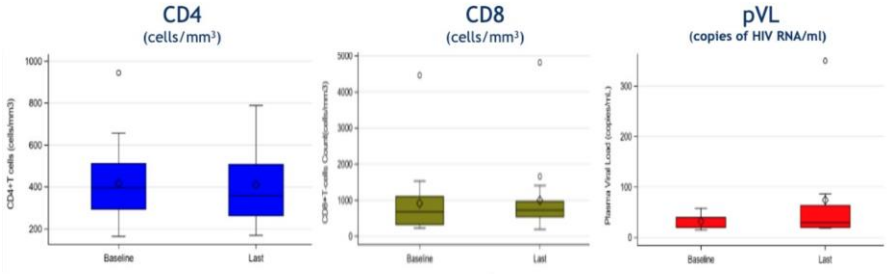
	n= 20
Age, median (range), y	54 (30-73)
Male sex, n (%)	16 (80%)
ECOG PS 0-1, n (%)	19 (95%)
Non smokers, n (%)	2 (10%)
Number of previous lines, median (range)	1 (0-3)
0, n (%)	8 (40%)
1, n (%)	8 (40%)
≥2, n (%)	4 (20%)
Tumor type, n (%)	
NSCLC Non Squamous	11 (55%)
NSCLC Squamous	3 (15%)
SCLC	1 (5%)
Melanoma	2 (10%)
Anal carcinoma	2 (10%)
Bladder carcinoma	1 (5%)
PD-L1 (TPS%)*, n (%)	
Negative (<1%)	11 (55%)
Low (1-49%)	1 (5%)
High (>50%)	3 (15%)

* 22C3 pharmDx kit

Adverse Events (AEs)

Non-Drug related AEs, n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Any	23 (75%)	10 (50%)	1 (5%)	1 (5%)	2 (10%)
Respiratory infection	1 (5%)	1 (5%)	1 (5%)	0	1 (5%)
Neurological	0	0	0	0	1 (5%)
Arterial ischemia	0	0	0	1 (5%)	0
Hypotension	0	3 (15%)	0	0	0
Fever	2 (10%)	2 (10%)	0	0	0
Arthromyalgia	11 (55%)	2 (10%)	0	0	0
Asthenia	9 (45%)	2 (10%)	0	0	0
Nausea-vomiting	5 (25%)	0	0	0	0
Constipation	2 (10%)	1 (5%)	0	0	0
Disphagia	2 (10%)	1 (5%)	0	0	0
Diarrhoea	2 (10%)	2 (10%)	0	0	0
Skin AEs	3 (15%)	0	0	0	0
Neutropenia	0	1 (5%)	0	0	0

T cell count and plasma viral load



	CD4 (cells/mm³)		CD8 (cells/mm³)		pVL (copies of HIV RNA/ml)	
	Baseline	Last	Baseline	Last	Baseline	Last
Mean (SD)	417 (181)	410 (202)	915 (945)	998 (1088)	32 (13)	74 (113)
Median	397	358	680	729	40	29
[Q1,Q3]	[294, 513]	[263,508]	[327, 1108]	[542, 972]	[20, 40]	[20, 63]
Min, Max	164, 945	169, 789	232, 4460	197, 4815	15, 58	19, 350

Inmunoterapia en VIH: DURVAST

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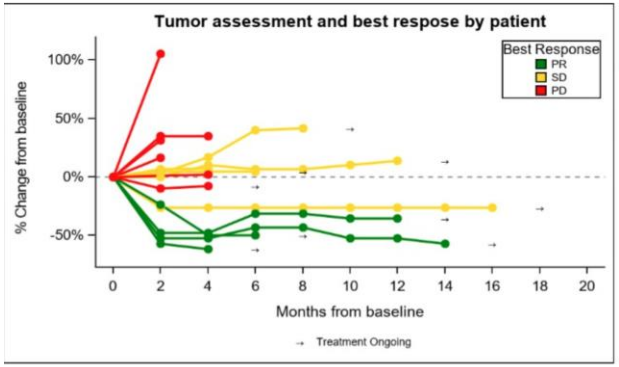
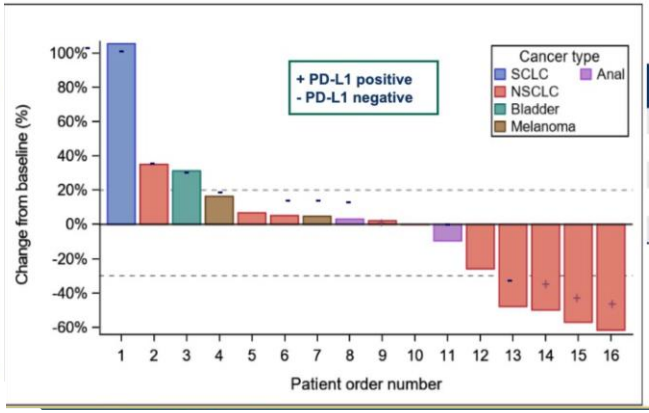
Tumor Response (RECIST v1.1)



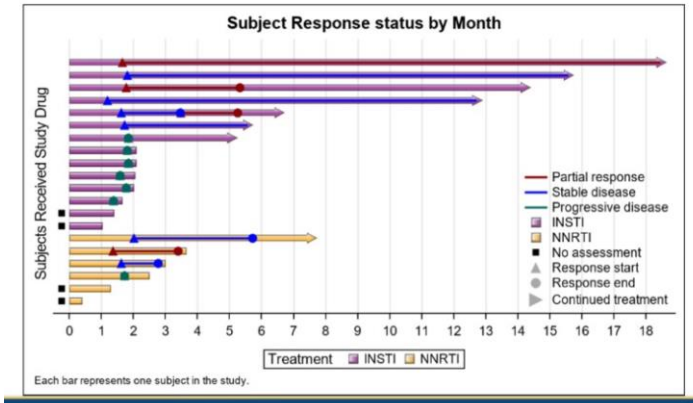
Response	All (n=20)
PR, n (%)	4 (20%)
SD, n (%)	5 (25%)
DCR, n (%)	8 (40%)
PD, n (%)	11 (55%)
RECIST	7 (35%)
NE	4 (20%)
DOR, months median (range)	6.5 (3.5-17 +)

Tumor Response (RECIST v1.1) according to PD-L1 expression



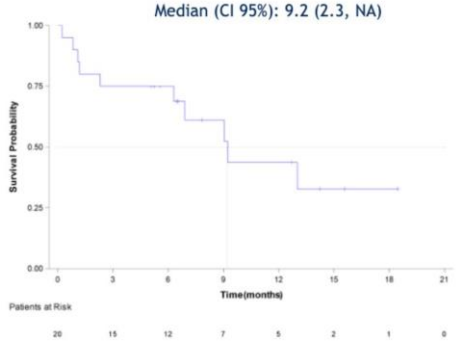
Response	PD-L1- (n=11)	PD-L1 + (n=4)
PR, n (%)	1 (7%)	3 (75%)
SD, n (%)	2 (18%)	1 (25%)
DCR, n (%)	3 (25%)	4 (100%)
PD, n (%)	5 (43%)	0
NE, n (%)	3 (25%)	

Time on treatment and time to first response

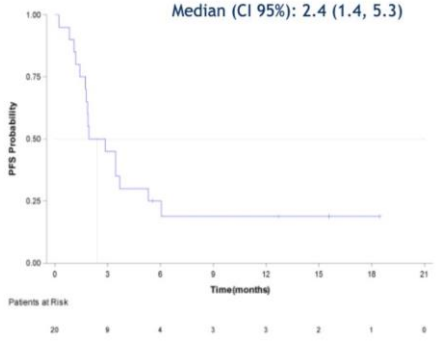


	Median (months)
INSTI	3.5
NNRTI	2.6
p (Wilcoxon)	0.44

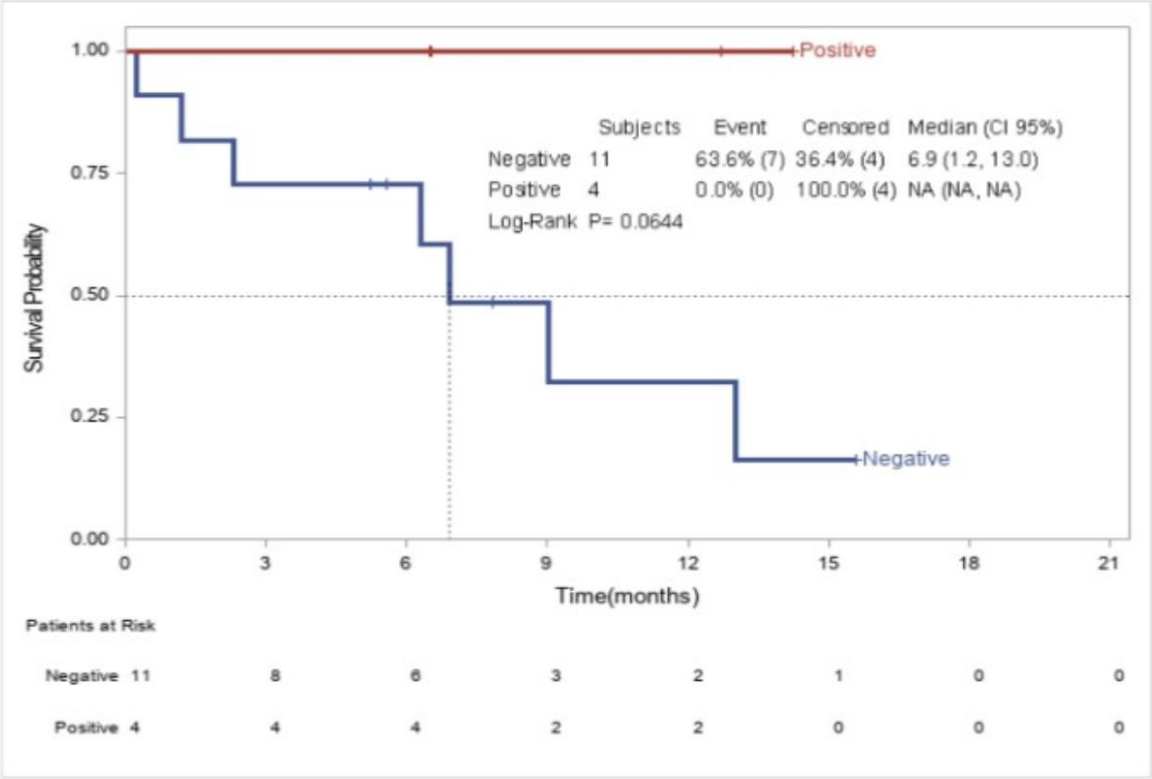
OS



PFS



Overall Survival according to PD-L1



Conclusions

- Durvalumab is feasible and safe in HIV-infected, stabilized, cancer patients
- Antitumoral activity was observed both in naïve and previously treated patients
- Our data suggest at least similar activity that has been found in cancer patients without HIV. Efficacy results of durvalumab allow confirmatory trials in this setting
- HIV infected persons should have access to cancer immunotherapy

Future Directions and Questions

1. The data from abstracts 2500/2501 are the only prospective data for anti-PD(L)-1 therapy in HIV+ patients
   - How can we learn more about patients with chronic infections – phase IV clinical trial vs standard care patients (ie flatiron health)
2. Are these data conclusive enough about safety and efficacy to stop excluding these patients from IO trials?
   - Per CTEP: Individuals known to be HIV-positive should not be arbitrarily excluded from participation in clinical cancer treatment trials.
   - Unique population set with some additional safety concerns (IRIS)
3. Can we identify other orphan diseases where IO may be beneficial?