LUNG CANCER UPDATES

AACR HIGHLIGHTS

29 MARZO - 3 ABRIL 2019

Iniciativa científica de:

GECP

Grupo Español de Cáncer de Pulmón

Spanish Lung Cancer Group

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NSCLC: Biomarcadores en Inmuno-Oncología

Dr. Santiago Ponce

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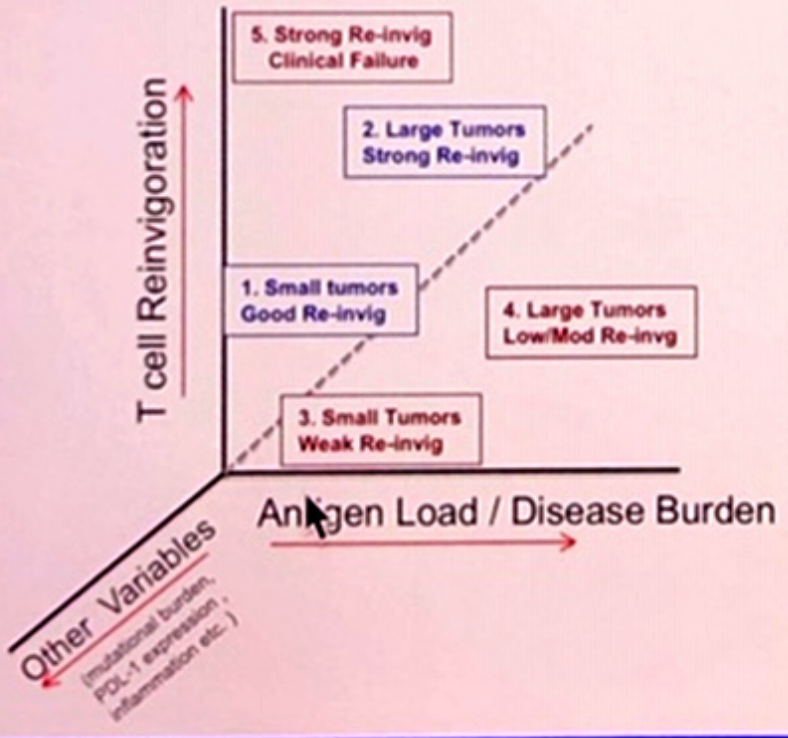
Disease burden and response to immunotherapy



1. Less Severe Exhaustion
   Small Tumors
2. Robust re-invigoration
   Dominant PD-1 regulation
3. Poor Priming, "cold" tumors
   Poor Immunogenicity
4. Dominant immunosuppression
   Severe exhaustion
   Poor re-invigoration
   Secondary checkpoints
5. Tumor Escape

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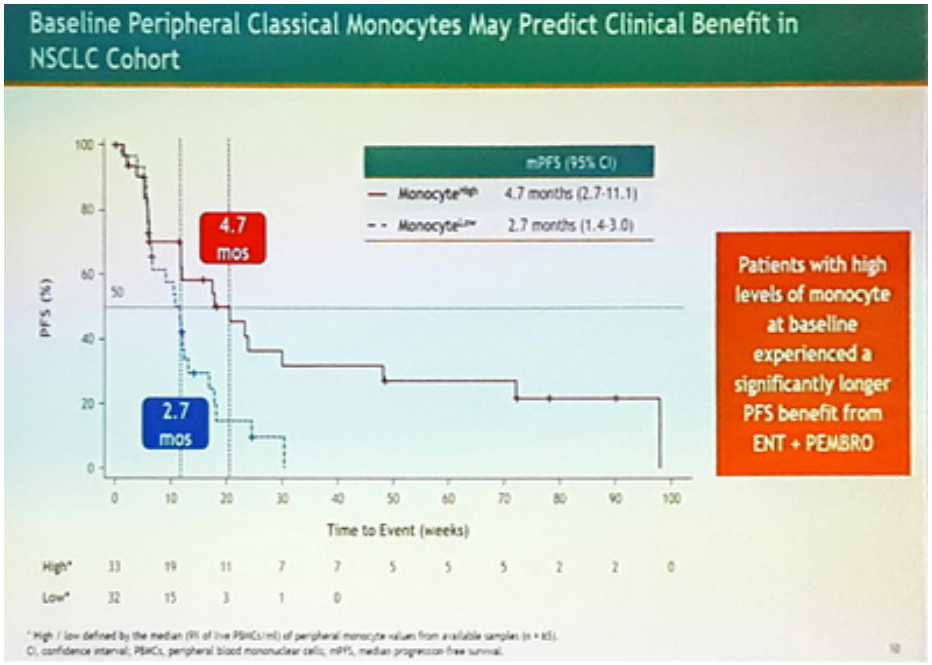
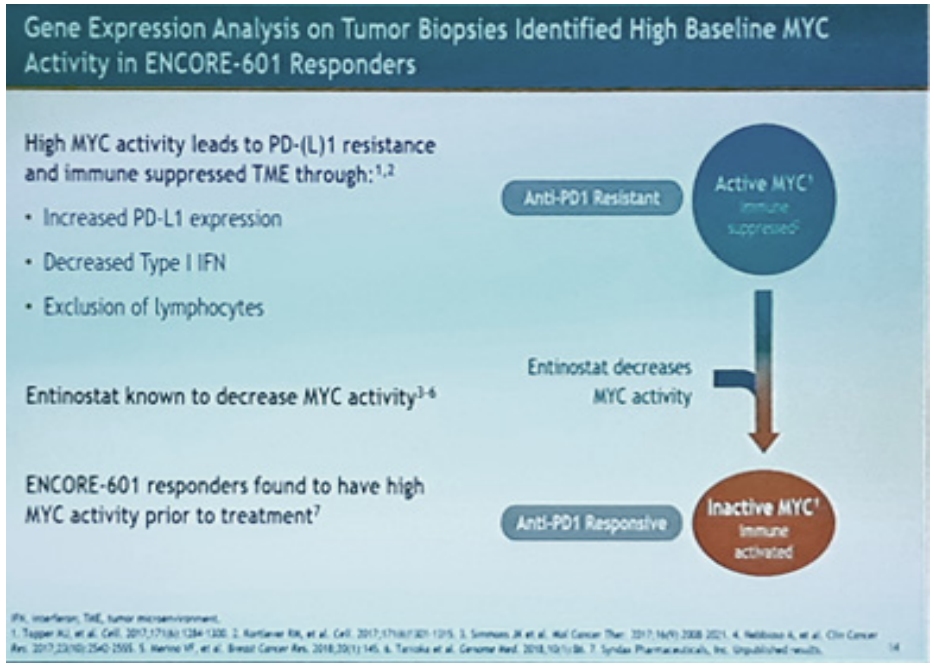




APX005M

Anti CD40 + Nivo

YTMA404 cohort

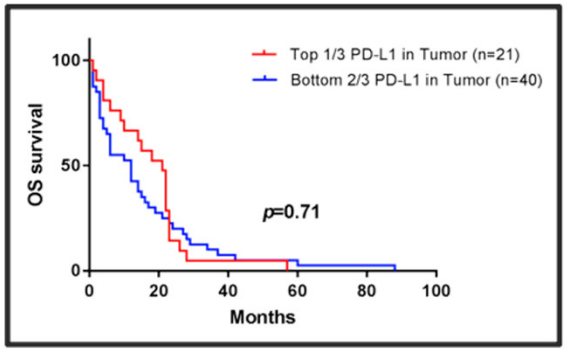
Characteristic	N (%)
Total	81
Gender	
Male	43 (53.1)
Female	38 (46.9)
Age	
< 70 yo	42 (51.9)
>= 70 yo	39 (48.1)
ECOG performance status	
0	7 (8.6)
1	63 (77.8)
2	10 (12.3)
3	1 (1.2)
Smoking history	
Never smoker	14 (17.3)
Current smoker	18 (22.2)
Former smoker	48 (59.3)
*Missing	1
Histology	
Adenocarcinoma	61 (75.3)
Squamous-cell carcinoma	15 (18.5)
Large-cell carcinoma	4 (4.9)
Adeno-squamous carcinoma	1 (1.2)
Stage	
III	2 (2.5)
IV (M1a)	21 (25.9)
IV (M1b)	11 (13.6)
IV (M1c)	47 (58)
Recurrent disease	
Yes	32 (39.5)
No	49 (60.5)

IT regimen	N (%)
Total	81
Nivolumab	57 (70.4)
Pembrolizumab	5 (6.2)
Atezolizumab	5 (6.2)
Nivolumab + Ipilimumab	5 (6.2)
Durvalumab + Tremelimumab	5 (6.2)
Carboplatin + Paclitaxel + Atezolizumab	2 (2.5)
Atezolizumab + Epacadostat	1 (1.2)

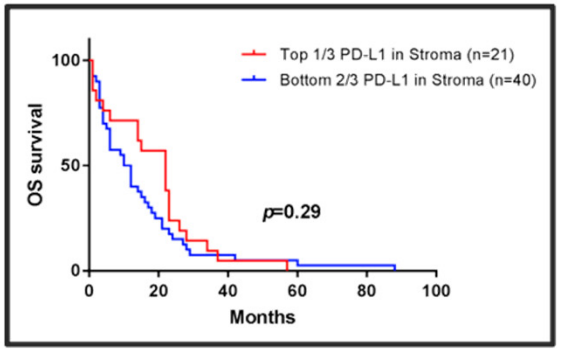
Moment of collection	N (%)
Total	81
Pre immunotherapy	73 (90.1)
Post immunotherapy - Acquired resistant specimen - Primary resistant specimen	8 (9.9) - 4 (4.9) - 4 (4.9)

67 patients with mono-therapy including 62 with pre-treatment biopsy available for study

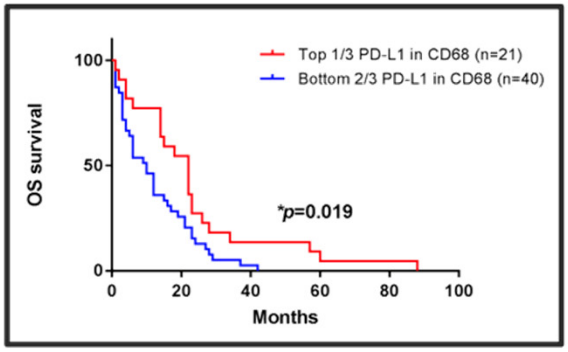
PD-L1 in tumor compartment



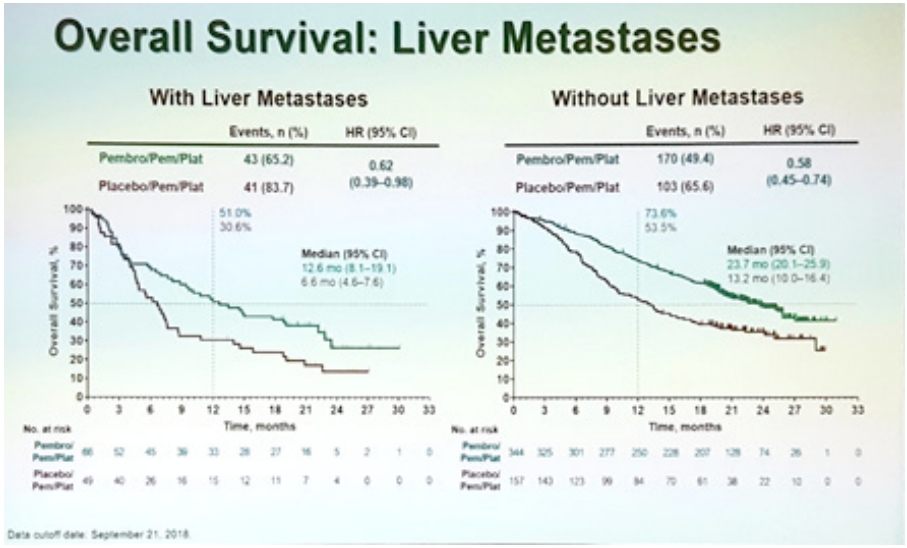
PD-L1 in stromal compartment

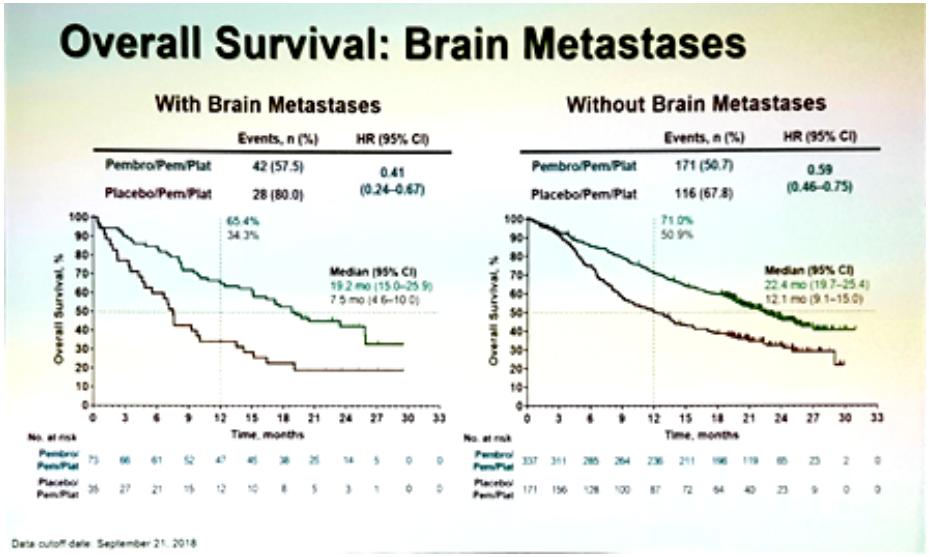


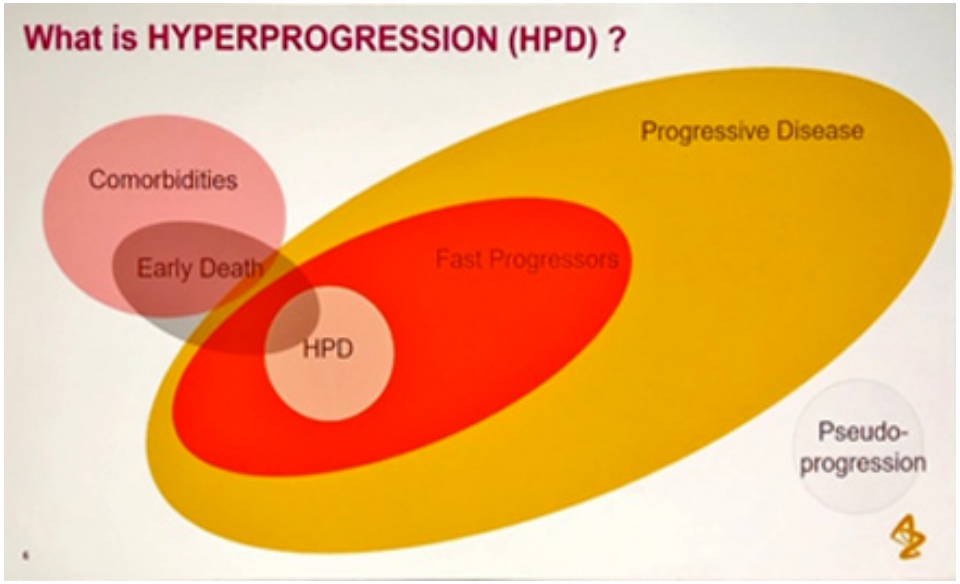
PD-L1 in macrophages



AQUA Analysis of Ultimapper intensity


Overall Survival: Liver Metastases
With Liver Metastases
Events, n (%)
HR (95% CI)
Pembro/Pem/Plat 43 (65.2)
Placebo/Pem/Plat 41 (83.7)
0.62 (0.39–0.98)
51.0%
30.6%
Median (95% CI)
12.6 mo (8.1–19.1)
6.6 mo (4.6–7.6)
Without Liver Metastases
Events, n (%)
HR (95% CI)
Pembro/Pem/Plat 170 (49.4)
Placebo/Pem/Plat 103 (65.6)
0.58 (0.45–0.74)
73.6%
53.5%
Median (95% CI)
23.7 mo (20.1–25.9)
13.2 mo (10.0–16.4)
Overall Survival, %
Time, months
No. at risk
Data cutoff date: September 21, 2018


Overall Survival: Brain Metastases
With Brain Metastases
Events, n (%)
HR (95% CI)
Pembro/Pem/Plat 42 (57.5)
Placebo/Pem/Plat 28 (80.0)
0.41 (0.24–0.67)
65.4%
34.3%
Median (95% CI)
19.2 mo (15.0–25.9)
7.5 mo (4.6–10.0)
Without Brain Metastases
Events, n (%)
HR (95% CI)
Pembro/Pem/Plat 171 (50.7)
Placebo/Pem/Plat 116 (67.8)
0.59 (0.46–0.75)
71.0%
50.9%
Median (95% CI)
22.4 mo (19.7–25.4)
12.1 mo (9.1–15.0)
Overall Survival, %
Time, months
No. at risk
Data cutoff date: September 21, 2018



Papers with different Criteria

	Champiat et al. Clin. Cancer Research 2016	Kato et al. Clin. Cancer Research 2017	Saâda-Bouzid et al. Annals of Oncology 2017	Ferrara et al. Jama Onc 2018	Lo Russo Clin. Cancer Research 2018	Gandara D LBA ESMO IO 2018
Population	N = 131 Metastatic cancers phase 1 trials PD1 or PD-L1 inhibitors monotherapy	N = 155 Metastatic cancers with molecular profiling CTLA-4, PD-1/PD-L1 inhibitors or other investigational agents	N = 34 Recurrent and/or Metastatic head and neck squamous cell carcinoma PD-1/PD-L1 inhibitors	N = 406 Advanced NSCLC PD-1/PD-L1 inhibitors + IO combo	N = 187 Advanced NSCLC PD-1/PD-L1 inhibitors + IO combo	N = 850 Advanced NSCLC Ateso vs Docetaxel
Criteria	RECIST PD at first evaluation & TGR EXP/TGR Ratio ≥ 2	TTF <2 months >50% increase in tumor burden >2-fold increase in "progression pace"	Acceleration of tumor growth kinetics (TGK) TGK ratio (TGK_2) ≥2	RECIST PD at first evaluation & TGR IO-TGR pre-IO > 50%	≥ 50% increase in SLD ≤ 6 weeks TTF<2 months + New lesions + ECOG PS deterioration	≥ 50% increase in SLD ≤ 6 weeks Early deaths
HPD rate	9% (12/131)	6% (6/102)	29% (10/34)	14% (56/406)	25.7% (39/187)	10% (44/425)
Associated factors	Age (64 vs 55, p = 0.007)	All analysis were performed for TTF < 2months only, no clinical correlation MDM2/MDM4 EGFR	Regional recurrence (TGKR2: 90% vs TGKR<2 : 37%, p=0.008)	Metastatic sites > 2 (3% vs 25%, p = 0.003)	No clinical association CD33 CD163 PD-L1 MDM2/MDM4, EGFR	NO FP