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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GECP
lung cancer research

Mantenimiento, tratamiento de KRAS+ e inhPARP

Dr. Javier Garde

Día 3

Con la colaboración de:

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9002: ECOG-ACRIN 5508

ECOG-ACRIN 5508 Study Scheme

Advanced Non-Squamous NSCLC
PS 0/1
No Prior Therapy

Carboplatin
Paclitaxel
Bevacizumab
X 4 Cycles
N=1516

CR/PR/SD

RANDOMIZE

- Bevacizumab N=287
- Pemetrexed N=294
- Bevacizumab + Pemetrexed N=293

Stratification factors:
Sex (Male vs. female)
Best response to Induction therapy (CR/PR vs. SD)
Stage (IIIB vs. IV M1a vs. IV M1b vs. recurrent)
Smoking status (never vs. ever)

Dose information
Carboplatin AUC=6
Paclitaxel 200 mg/m²
Pemetrexed 500 mg/m²
Bevacizumab 15 mg/Kg

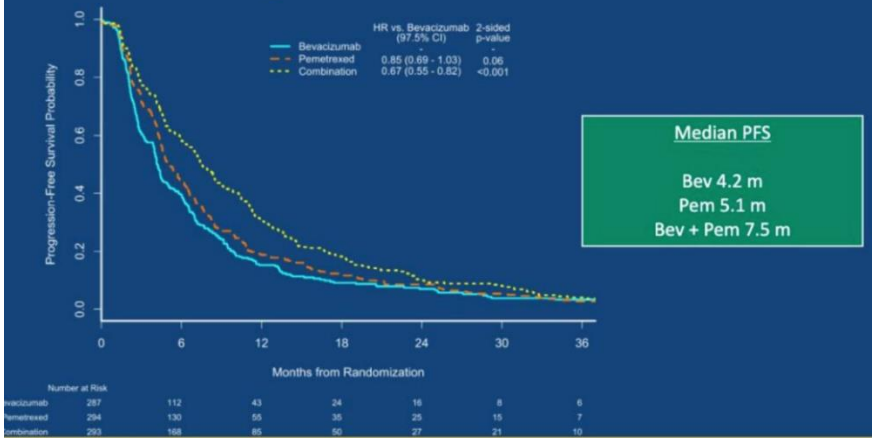
Efficacy

Chemo + Bev Induction
- RR 30%
- Median survival 13.1 m

Maintenance
- RR
  - Bev- 13%
  - Pem- 19%
  - Pem + Bev- 21%

Median follow-up 60 m in maintenance phase

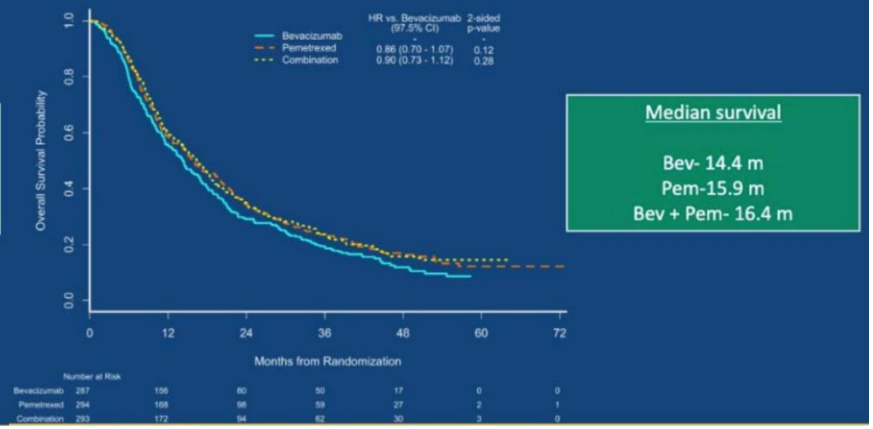
Progression-free Survival



Median PFS

Bev 4.2 m
Pem 5.1 m
Bev + Pem 7.5 m

Overall Survival



Median survival

Bev- 14.4 m
Pem-15.9 m
Bev + Pem- 16.4 m

Abstract 9002 Suresh S et al. ECOG-ACRIN 5508: Pemetrexed, bevacizumab or the combination as maintenance therapy for advanced non-squamous NSCLC. ,

9002: ECOG-ACRIN 5508

Treatment-related Grades 3/4 Toxicity

	Grade 3/4 toxicity (%)		
Treatment Group	Bevacizumab	Pemetrexed	Bevacizumab + Pemetrexed
Anemia	2/0	7/0	6/<1*
Lymphopenia	1/0	4/1*	7/1*
Neutropenia	1/0	5/2*	8/3*
Leucopenia	0/0	4/1*	4/1*
Thrombocytopenia	0/0	2/1*	2/2*
Hyponatremia	2/0	2/0	4/<1
Fatigue	2/0	7/0*	8/0*
Proteinuria	4/0*	<1/0	3/0
Hypertension	16*	5/0	19/0
Worst degree	27/2	32/5	43/7*

Incudes treatment-related AE occurring in ≥ 4% of patients

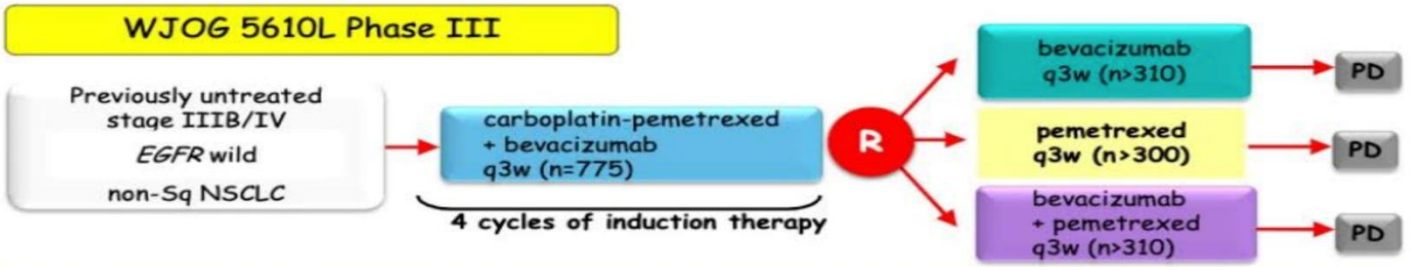
* Represents P value ≤ 0.02

- *Abstract 9002 Suresh S et al. ECOG-ACRIN 5508: Pemetrexed, bevacizumab or the combination as maintenance therapy for advanced non-squamous NSCLC,*

9003 COMPASS: Beva vs Beva-Pemetrexed

Study design

COMPASS was designed in 2009



- ✓ Primary endpoint: OS after randomization
- ✓ Secondary endpoints: PFS, OS and PFS from the 1st registration, safety
- ✓ Stratification factors: institution, histological type, response at randomization

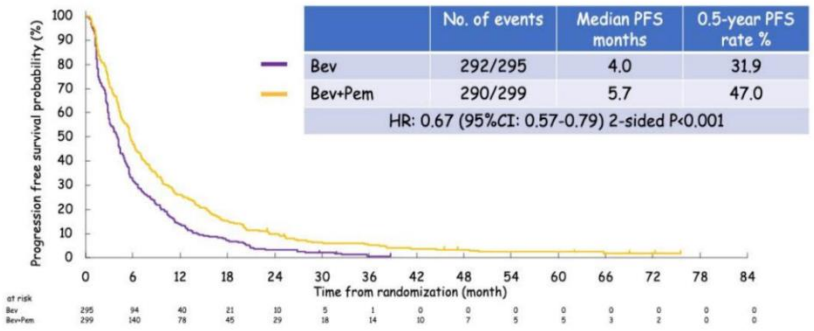
Toxicities grade 3 or greater

	Induction phase		Maintenance phase			
	Car+Pem+Bev n=895		Bev n=295		Bev+Pem n=299	
Anemia	172	19.2%	1	0.3%	14	4.7%
White blood cell count decreased	164	18.3%	0	0.0%	16	5.4%
Neutrophil count decreased	379	42.3%	3	1.0%	42	14.0%
Platelet count decreased	277	30.9%	1	0.3%	3	1.0%
Hypertension	111	12.4%	49	16.6%	35	11.7%
Anorexia	69	7.7%	1	0.3%	7	2.3%

Takashi S, et al. A randimize phase III study of continous maintenance bevacizumab with or without pemetrexed after induction therapy with carboplatin, pemetrexed, and bevacizumab for advanced non-squamous non-small cell lung cáncer withoyt sensitizing EGFR mutations: the COMPASS study

9003 COMPASS: Beva vs Beva-Pemetrexed

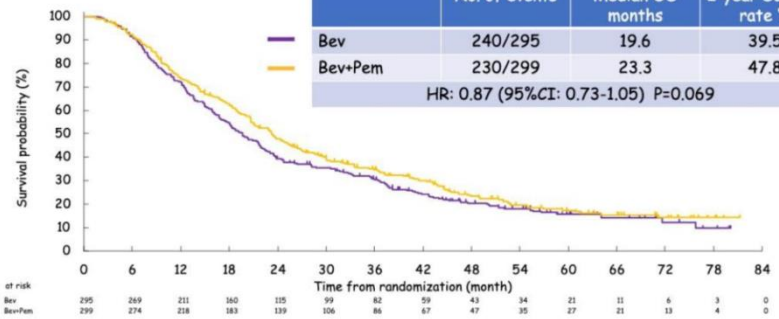
Progression-free survival after randomization



	No. of events	Median PFS months	0.5-year PFS rate %
Bev	292/295	4.0	31.9
Bev+Pem	290/299	5.7	47.0
HR: 0.67 (95%CI: 0.57-0.79) 2-sided P<0.001			

The median follow-up time from randomization was 59.9 months (95%CI, 56.4-62.5 months)

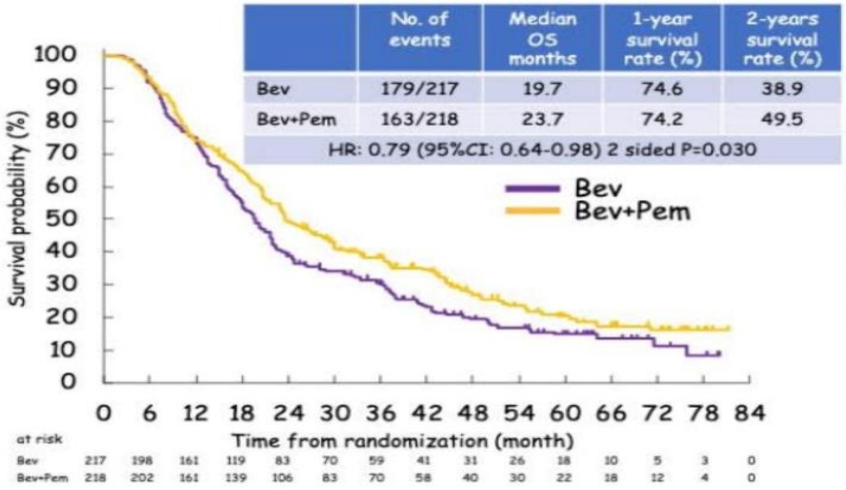
Overall survival from randomization :Primary endpoint



	No. of events	Median OS months	2-year Survival rate %
Bev	240/295	19.6	39.5
Bev+Pem	230/299	23.3	47.8
HR: 0.87 (95%CI: 0.73-1.05) P=0.069			

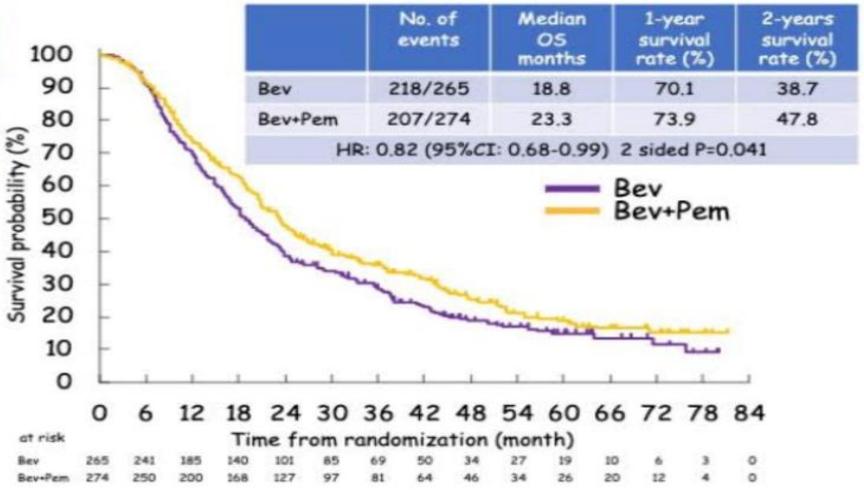
Estimated median OS of Bev : 13 months Expected median OS of Bev+Pem arm : 16.5 months

- **<70 years old**



	No. of events	Median OS months	1-year survival rate (%)	2-years survival rate (%)
Bev	179/217	19.7	74.6	38.9
Bev+Pem	163/218	23.7	74.2	49.5
HR: 0.79 (95%CI: 0.64-0.98) 2 sided P=0.030				

- **wild-type *EGFR***



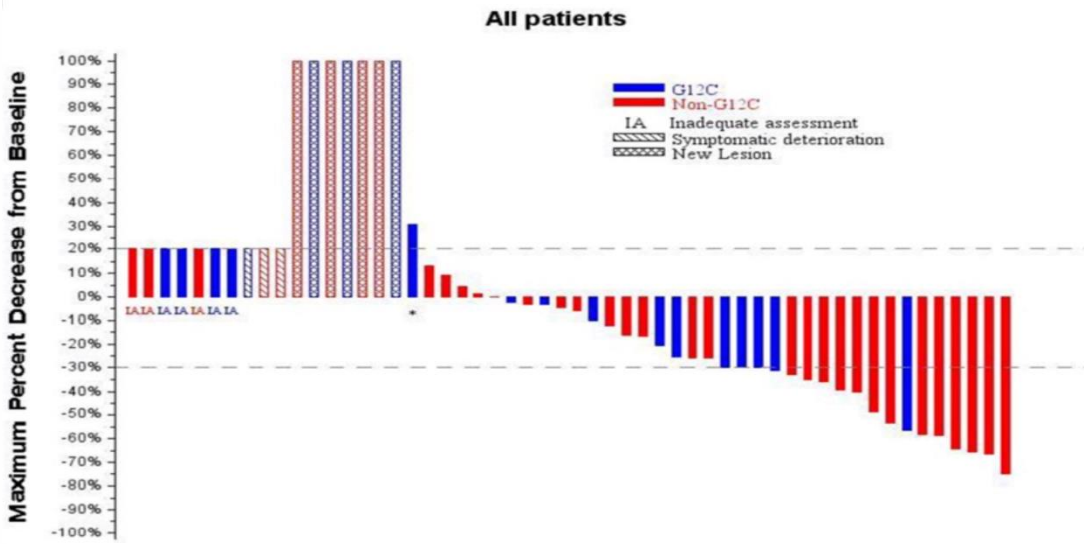
	No. of events	Median OS months	1-year survival rate (%)	2-years survival rate (%)
Bev	218/265	18.8	70.1	38.7
Bev+Pem	207/274	23.3	73.9	47.8
HR: 0.82 (95%CI: 0.68-0.99) 2 sided P=0.041				

Takashi S, et al. A randimize phase III study of continous maintenance bevacizumab with or without pemetrexed after induction therapy with carboplatin, pemetrexed, and bevacizumab for advanced non-squamous non-small cell lung cáncer withoyt sensitizing EGFR mutations: the COMPASS study

9021: KRAS+ Docetaxel + Trametinib

Docetaxel 75 mg/m² IV every 3 weeks
+
Trametinib 2mg daily, PO
+
G-CSF every cycle
Treatment till progression

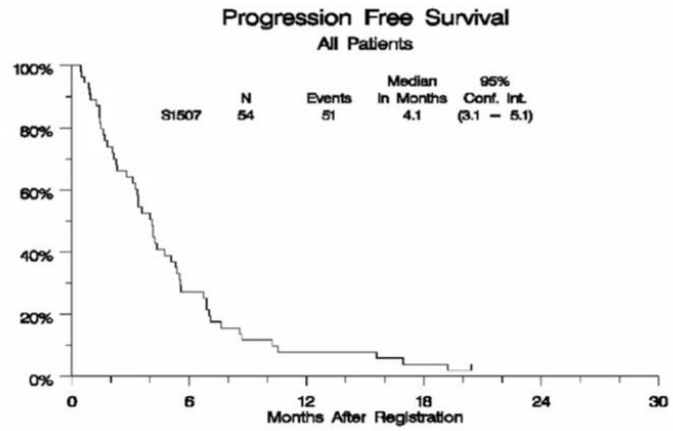
→ *KRAS* + NSCLC 1 or 2 prior regimens

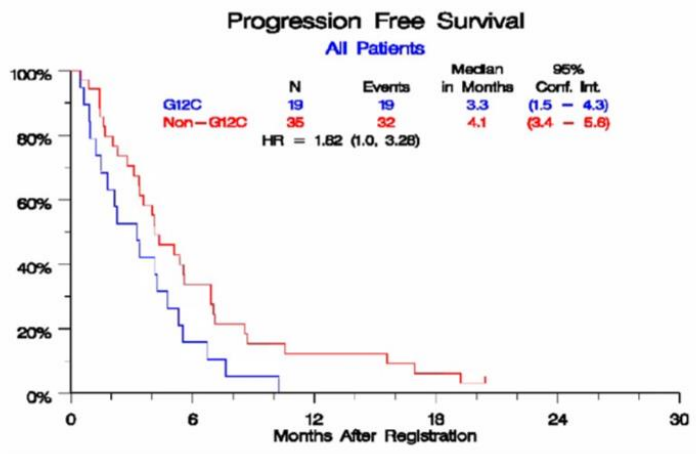


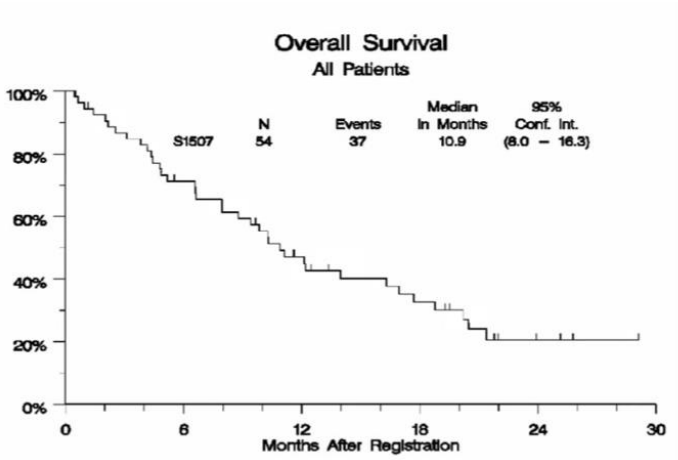
	All	G12C	Non-G12C
Response	33% (95% CI: 21%-47%)	26% (95% CI: 9%-51%)	37% (95% CI: 21%-55%)
PFS (median in months)	4.1 (95% CI- 3.1-5.1)	3.3 (95% CI: 1.5-4.3)	4.1 (95% CI: 3.4-5.6)
OS (median in months)	11.1 (95% CI- 8-17)	8.8 (95% CI: 4.9-12.1)	16.3 (95% CI: 9.9-17.7)

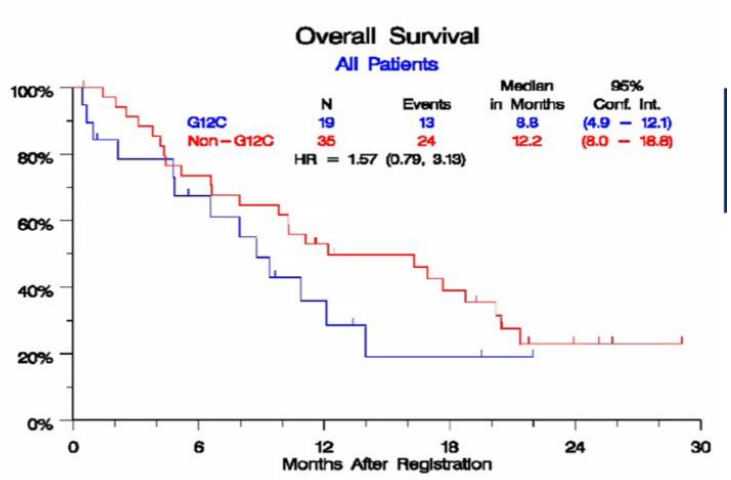
ABSTRACT 9021, Shirish et al, S1507: Phase II study o docetaxel and trametinib in patients with G12C or non-G12C KRAS mutation positive (+) recurrent non-small cell lung cáncer (NSCLC)

9021: KRAS+ Docetaxel + Trametinib









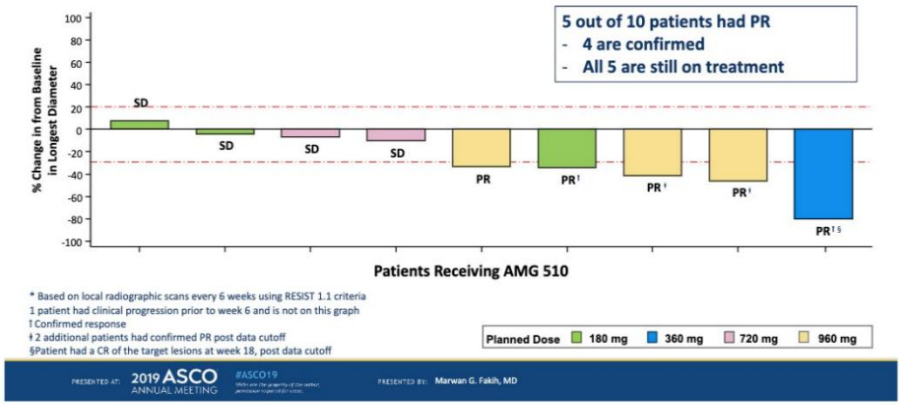
ABSTRACT 9021, Shirish et al, S1507: Phase II study o docetaxel and trametinib in patients with G12C or non-G12C KRAS mutation positive (+) recurrent non-small cell lung cáncer (NSCLC)

AMG 510: NSCLC KRAS 12C+

Phase 1 Study Evaluating the Safety, Tolerability, Pharmacokinetics (PK) and Efficacy of AMG 510, a Novel Small Molecule KRAS^{G12C} Inhibitor, in Advanced Solid Tumors

Marwan G Fakih, MD;[1] Bert Howard O'Neil, MD;[2] Timothy J Price, MBBS, FRACP;[3] Gerald S Falchook, MD;[5] Jayesh Desai, MBBS, FRACP;[6] James Kuo, MBBS, FRACP;[7] Ramaswamy Govindan, MD;[8] Erik Rasmussen, MS;[4] Phuong Khanh Morrow, MD;[4] Jude Ngang, PharmD;[4] Haby Henary, MD;[4] David Hong, MD[9]

NSCLC: Best Tumor Response* (n=10)



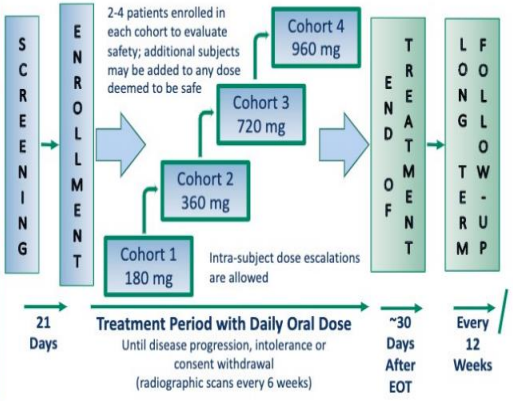
AMG 510 First in Human Study Design

This is a multicenter, open-label, phase 1, first in human study (NCT 03600883) in adult patients with locally advanced or metastatic *KRAS*^{G12C} mutant solid tumors

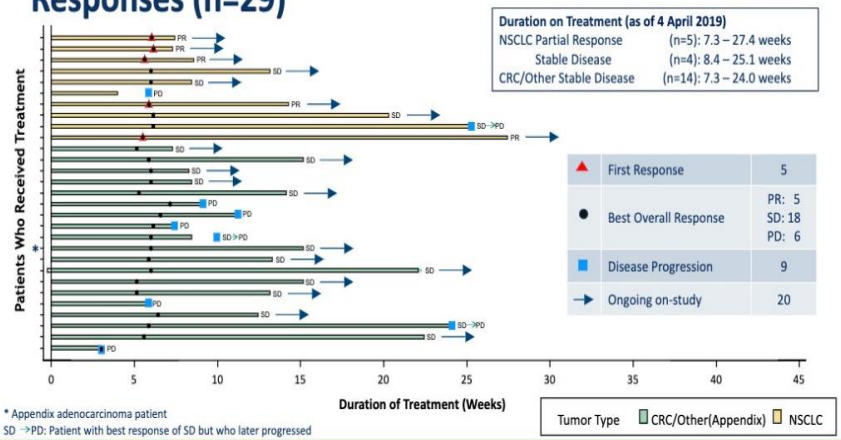
Key Eligibility Criteria
- Documented locally-advanced or metastatic *KRAS*^{G12C} measurable or evaluable solid tumors
- Received prior standard therapy appropriate for tumor type and stage of disease
- No active brain metastases

Primary Endpoints
- Safety and tolerability including the incidence of AEs and DLTs

Key Secondary Endpoints
- PK, best response
- Objective response rate , duration of response and duration of stable disease and PFS



Duration of Treatment by Tumor Types and Responses (n=29)



* Appendix adenocarcinoma patient
SD →PD: Patient with best response of SD but who later progressed

9022 Talazoparib en Ca Epidermoide HRRD+

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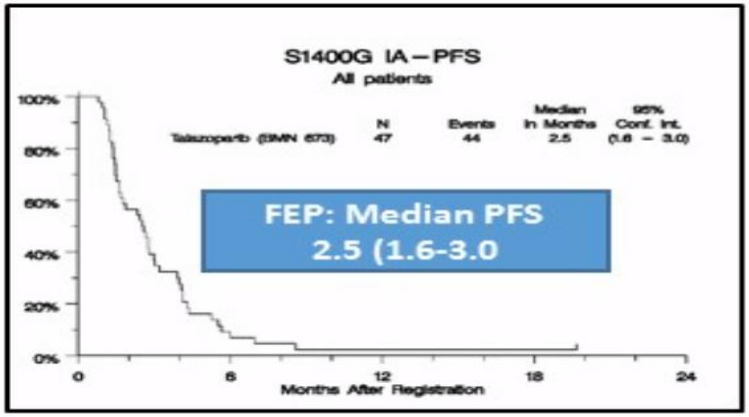
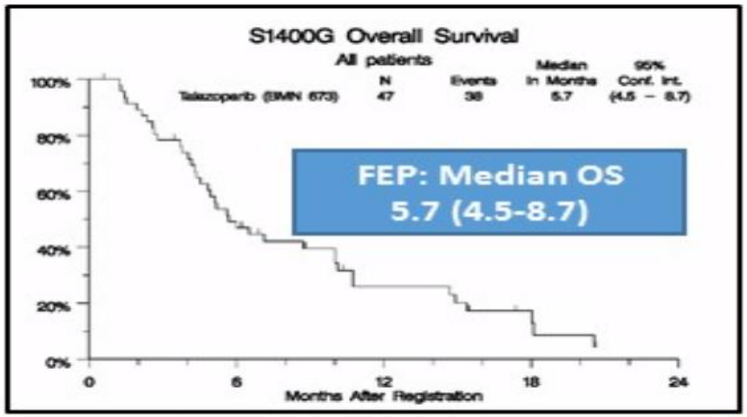
Patients Characteristics	
Demographics	
Age (median)	66.7 (37.5-82.1)
Male/Female	39/8 (83%/17%)
Black/White	7/40 (15%/85%)
# of prior lines	
0	11 (23%)
1	13 (28%)
≥2	23 (49%)
PS 0/1	10/37 (21%/79%)
Efficacy by Biomarker Subgroup	
FEP:N=47	
ORR	5 (11%; 95%CI: 4-23)
DCR	24 (51%; 95%CI: 36-66)
PAP: N=24 (51%)	
ORR	1 (4%; 95%CI: 0-21)
DCR	13 (54%; 95%CI: 33-74)

Frequency of HRRD gene mutations		
FANCM***	7	15%
FANCD2	1	2%
FANCF	2	4%
FANCA	4	9%
BRCA1	6	13%
BRCA2*	9	19%
BRIP1	2	4%
ATM	3	6%
ATR	4	9%
PALB2	3	6%
CHEK1*	3	6%
CHEK2	2	4%
RPA1	1	2%
NBN	2	4%
>1 mutation	2	4%
(* denotes patients with objective response)		

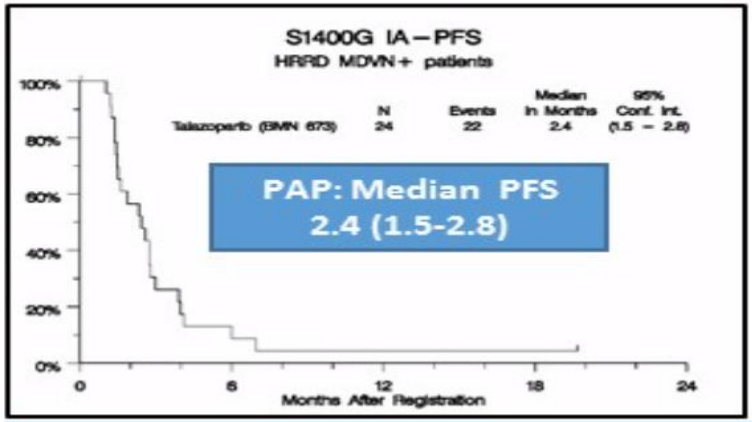
9022. Taofeek et al, A phase II study of talazopanib in pstients withh homologus recombination repair deficiency (HRRD) positive stage IV squamous cell lung cáncer (Lung-Map substtudy)

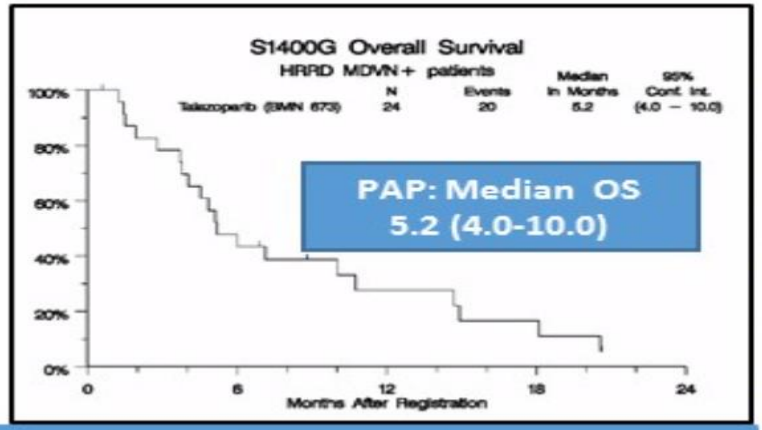
9022 Talazoparib en Ca Epidermoide HRRD+





Full Evaluable Population (FEP) with mutation in any study-defined HRRD genes





Primary Analysis Population (PAP) with mutation in *ATM, ATR, BRCA1, BRCA2, PALB2 genes*