Best of ASCO 2019: Lung and Genitourinary Cancers

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August 28, 2019

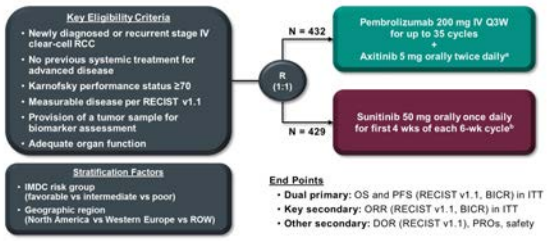
- *Research Funding*: Merck, GeneCentric, Bristol-Myers Squibb, X4 Pharmaceuticals

Disclosures

2019 in GU Cancers

- Kidney Cancer
  - First-line IO/VEGF combinations
  - "Adjuvant" pazopanib after metastasectomy
- Bladder Cancer
  - Post-platinum, post-checkpoint options
- Prostate Cancer
  - The explosion of options for hormone sensitive metastatic prostate cancer
  - M0 CRPC

KEYNOTE-426 Study Design



[a]Axitinib dose could be increased to 7 mg, then 10 mg, twice daily if safety criteria were met; dose could be reduced to 3 mg, then 2 mg, twice daily to manage toxicity. [b]Sunitinib dose could be decreased to 37.5 mg, then 25 mg, once daily for the first 4 wks of each 6-wk cycle to manage toxicity.
BICR, blinded independent central radiologic review; DOR, duration of response; PROs, patient-reported outcomes; ROW, rest of world.
KEYNOTE-426 is a randomized, open-label, phase 3 study (ClinicalTrials.gov identifier NCT02853331).

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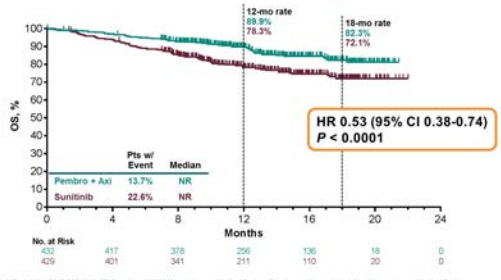
KEYNOTE-426: OS in the ITT Population



From Rini BI et al. *N Engl J Med* 2019;380:1116–27. Copyright © 2019 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

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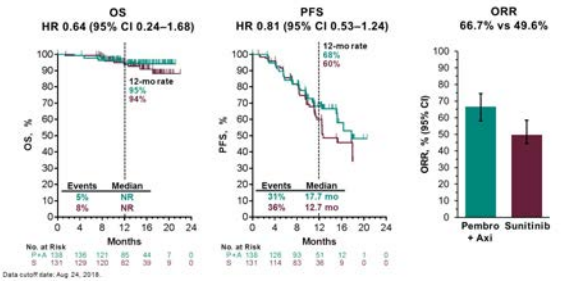
Pembrolizumab plus Axitinib for mRCC

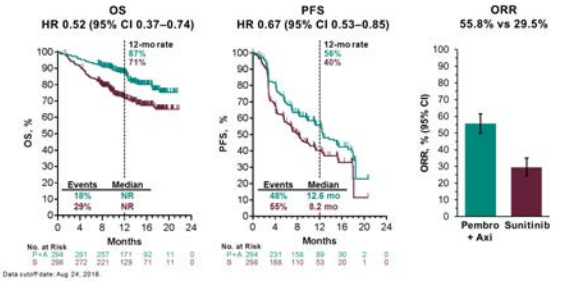
- Other key findings from KEYNOTE-426[1]
  - PFS: HR 0.69 ($P < 0.001$)
  - ORR: 59.3% vs 35.7% ($P < 0.001$)
  - Benefit observed across subgroups, including the IMDC favorable, intermediate, and poor risk groups and in PD-L1–expressing and non-expressing tumors
  - Manageable safety profile
- Combination of pembrolizumab and axitinib approved by the FDA for first-line treatment of advanced RCC

Rini BI et al. *N Engl J Med* 2019;380:1116–27.

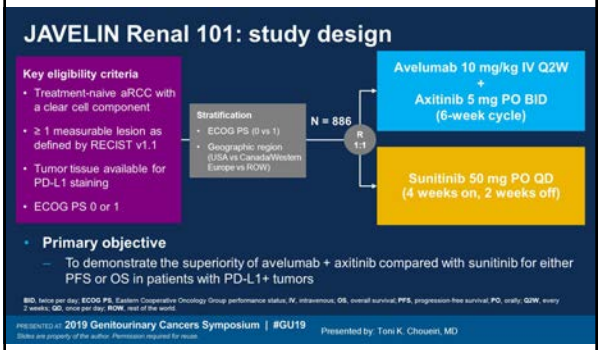
IMDC Favorable Risk: OS, PFS, and ORR



IMDC Intermediate/Poor Risk: OS, PFS, and ORR



JAVELIN Renal 101: study design



- **Primary objective**
  - To demonstrate the superiority of avelumab + axitinib compared with sunitinib for either PFS or OS in patients with PD-L1+ tumors

BID, twice per day; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; OS, overall survival; PFS, progression-free survival; PO, orally; Q2W, every 2 weeks; QD, once per day; ROW, rest of the world

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Presented By Toni Choueiri at 2019 Genitourinary Cancers Symposium

JAVELIN Renal 101 efficacy summary[1]

	PD-L1+ group (N = 560)		Overall population (N = 886)	
	Avelumab + axitinib (N = 270)	Sunitinib (N = 290)	Avelumab + axitinib (N = 442)	Sunitinib (N = 444)
PFS per IRC				
Median, months	13.8	7.2	13.8	8.4
95% CI	11.1, NE	5.7, 9.7	11.1, NE	6.9, 11.1
Benefit vs sunitinib (HR; P value)	0.61; P < .0001	-	0.69; P = .0001	-
ORR per IRC, %	55.2	25.5	51.4	25.7
95% CI	49.0, 61.2	20.6, 30.9	46.6, 56.1	21.7, 30.0
PFS per investigator assessment				
Median, months	13.3	8.2	12.5	8.4
95% CI	9.8, NE	6.9, 8.5	11.1, 15.2	8.2, 9.7
Benefit vs sunitinib (HR; P value)	0.51; P < .0001	-	0.64; P < .0001	-
ORR per investigator assessment, %	61.9	29.7	55.9	30.2
95% CI	55.8, 67.7	24.5, 35.3	51.1, 60.6	25.9, 34.7

IRC, independent review committee; NE, not estimable; ORR, objective response rate.
Data cutoff date: June 25, 2018; median follow-up, 12.0 months (avelumab + axitinib) and 11.5 months (sunitinib).
1. Motzer RJ, et al. ESMO 2018;LBA6_PR.

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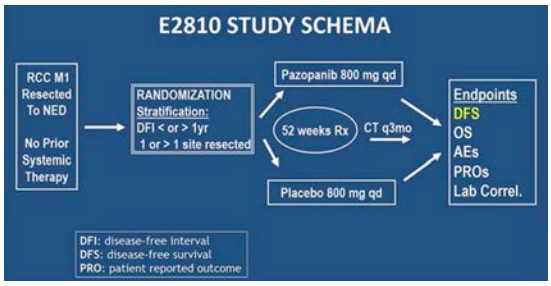
So which 1L treatment to pick?

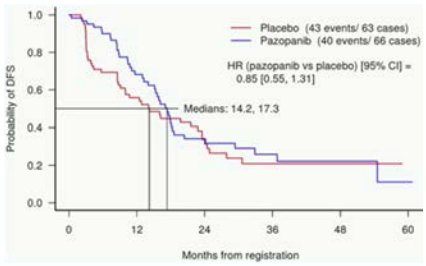
	Pembrolizumab + Axitinib vs Sunitinib	Avelumab + Axitinib vs Sunitinib	Ipilimumab + Nivolumab vs Sunitinib
IMDC risk group			
Favorable	31.2%	21.4%	23%
Intermediate	56.2%	61.8%	61%
Poor	12.6%	16.2%	17%
PDL1 "positive"	60.5%	63.2%	63.2%
Overall survival			
HR for death	0.53	0.78	0.68
P value	<0.0001	0.14	<0.001
Median PFS (mo)			
Combo therapy	15.1	13.8	12.4
Sunitinib	11.1	8.4	12.3
ORR (%)	59.3%	51.4%	39.0%
CR (%)	5.8%	3.4%	10.2%
Median f/u (mo)	12.8	11.6	25.2

Adapted from Escudier, NEJM 380;12 March 2

E2810 STUDY SCHEMA



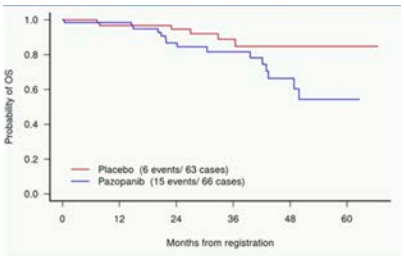
Pazopanib did not improve disease-free survival



Median follow-up 30 months

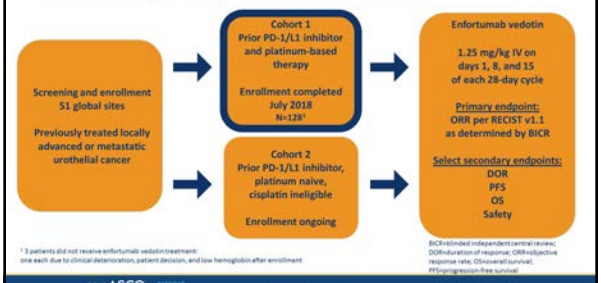
36 month DFS:
Pazopanib 26%
Placebo 22%

Overall survival by blinded treatment arm



Hazard Ratio for OS was 2.65 (1.02, 6.9) favor of placebo (p=0.05)

EV-201: Single-Arm, Pivotal Phase 2 Trial



[1] 3 patients did not receive enfortumab vedotin treatment: one each due to clinical deterioration, patient decision, and low hemoglobin after enrollment

BICR=blinded independent central review; DOR=duration of response; ORR=objective response rate; OS=overall survival; PFS=progression-free survival

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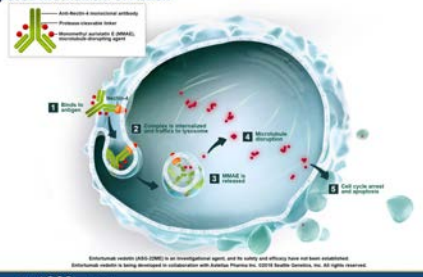
Enfortumab Vedotin: Nectin-4 Targeted Therapy

Proposed Mechanism of Action



Enfortumab vedotin (ASG-22ME) is an investigational agent, and its safety and efficacy have not been established.
Enfortumab vedotin is being developed in collaboration with Astellas Pharma Inc. ©2018 Seattle Genetics, Inc. All rights reserved.

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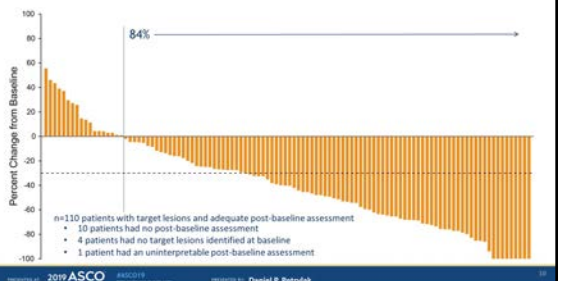
EV-201: Cohort 1 Change in Tumor Measurements per BICR



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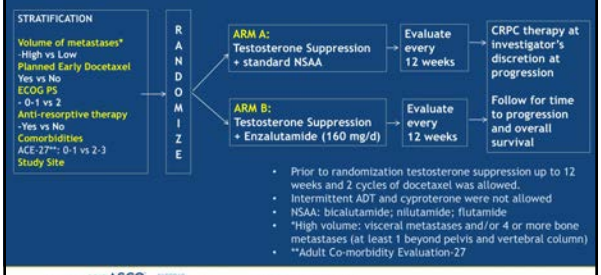
ENZAMET Treatment



- Prior to randomization testosterone suppression up to 12 weeks and 2 cycles of docetaxel was allowed.
- Intermittent ADT and cyproterone were not allowed
- NSAA: bicalutamide; nilutamide; flutamide
- *High volume: visceral metastases and/or 4 or more bone metastases (at least 1 beyond pelvis and vertebral column)
- **Adult Co-morbidity Evaluation-27

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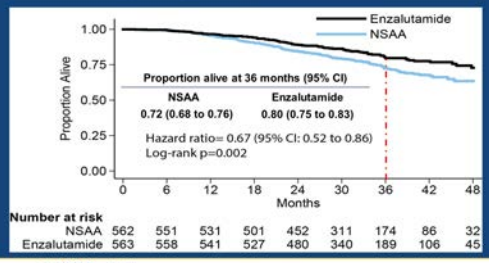
Primary endpoint: Overall survival



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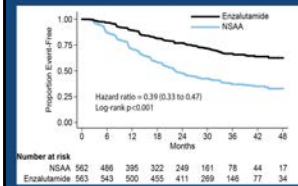
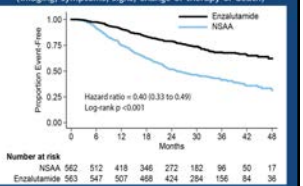
Secondary Endpoints: Progression-free survival (PCWG2)

Time to PSA rise, clinical progression or death



Time to clinical progression
(imaging, symptoms, signs, change of therapy or death)



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Abstract 5006

First Results From TITAN: a Phase 3 Double-Blind, Randomized Study of Apalutamide Versus Placebo in Patients With Metastatic Castration-Sensitive Prostate Cancer Receiving Androgen Deprivation Therapy

Kim N. Chi,[1] Neeraj Agarwal,[2] Anders Bjartell,[3] Byung Ha Chung,[4] Andrea Juliana Pereira de Santana Gomes,[5] Robert W. Given,[6] Álvaro Juárez Soto,[7] Axel S. Merseburger,[8] Mustafa Özgüroğlu,[9] Hirotsugu Uemura,[10] Dingwei Ye,[11] Kris Deprince,[12] Vahid Naini,[13] Jinhui Li,[13] Shinta Cheng,[14] Margaret K. Yu,[15] Ke Zhang,[13] Julie S. Larsen,[15] Sharon A. McCarthy,[14] Simon Chowdhury[16] on behalf of the TITAN investigators

[1]BC Cancer and Vancouver Prostate Centre, Vancouver, BC, Canada; [2]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT; [3]Skåne University Hospital, Lund University, Malmö, Sweden; [4]Yonsei University College of Medicine and Gangnam Severance Hospital, Seoul, South Korea; [5]Liga Norte Riograndense Contra O Cancer, Natal, Brazil; [6]Urology of Virginia, Eastern Virginia Medical School, Norfolk, VA; [7]Hospital Universitario de Jerez de la Frontera, Cadiz, Spain; [8]University Hospital Schleswig-Holstein, Campus Lübeck, Lübeck, Germany; [9]Istanbul University-Cerrahpaşa, Cerrahpaşa School of Medicine, Istanbul, Turkey; [10]Kindai University Faculty of Medicine, Osaka, Japan; [11]Fudan University Shanghai Cancer Center, Shanghai, China; [12]Janssen Research & Development, Beerse, Belgium; [13]Janssen Research & Development, San Diego, CA; [14]Janssen Research & Development, Raritan, NJ; [15]Janssen Research & Development, Los Angeles, CA; [16]Guy's, King's, and St. Thomas' Hospitals, and Sarah Cannon Research Institute, London, UK

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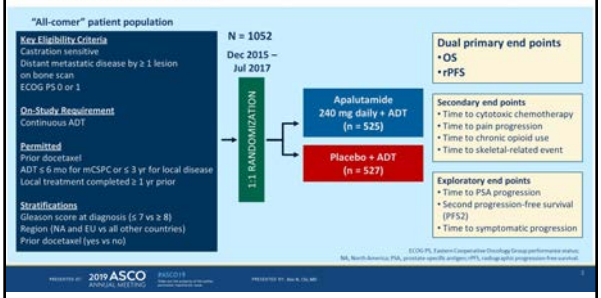
TITAN Study Design



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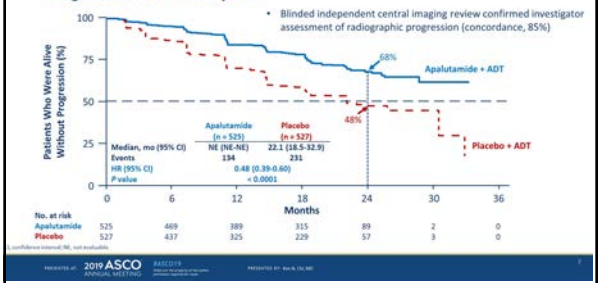
TITAN rPFS: Apalutamide Significantly Reduced Risk of Radiographic Progression or Death by 52%



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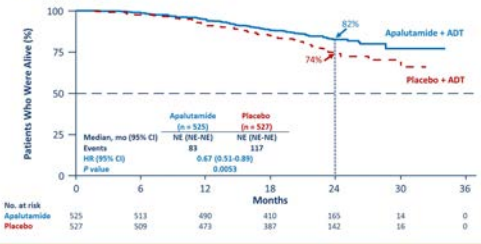
TITAN OS: Apalutamide Significantly Reduced the Risk of Death by 33%



Presented By Kim Chi at 2019 ASCO Annual Meeting

What to use in hormone sensitive disease?

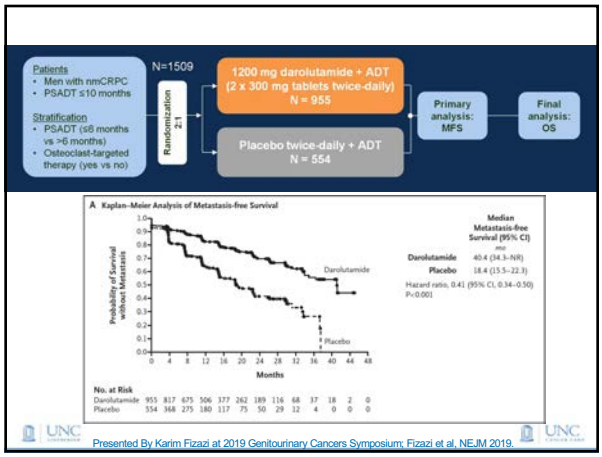
	CHAARTED (docetaxel)	LATITUDE (abiraterone/P)	ENZAMET (enzalutamide)	TITAN (apalutamide)
High volume disease, %	66%	100%	%	
rPFS, HR (95%CI)	0.62 (0.5-0.8)	0.47 (0.4-0.6)		
OS, low vol disease, HR (95%CI)	1.04 (0.7-1.6)	N/A		
OS, HR (95%CI)	0.72 (0.6-0.9)	0.66 (0.6-0.8)		
Discontinuation rate for AE		12%		
Grade >=3% AE	29.6%	63% vs 48%		
QoL scores	Worse at 3mos, better at 12 mos	Better than placebo		

CHAARTED, Sweeney et al, NEJM 2015
Latitude, Fizazi et al NEJM 2017
Enzamet, 2019 ASCO Annual Meeting
Titan, 2019 ASCO Annual Meeting

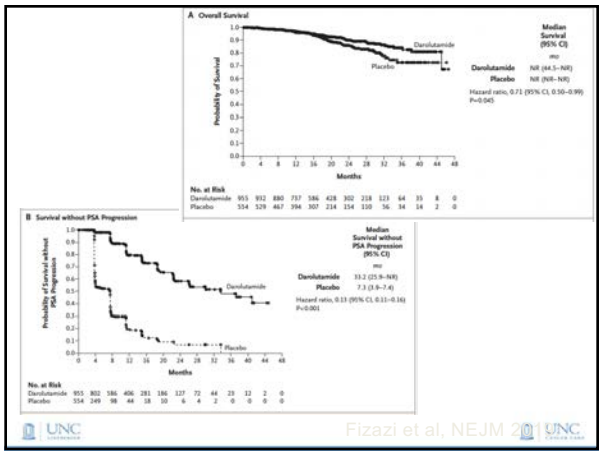
ARAMIS: Darolutamide in non-metastatic castration-resistant prostate cancer

- Androgen receptor inhibitor
- Structurally distinct from enza/apalutamide – less CNS toxicity since doesn't cross BBB and fewer drug interactions (not a CYP-inhibitor)
- Taken with food

Presented By Karim Fizazi at 2019 Genitourinary Cancers Symposium



Presented By Karim Fizazi at 2019 Genitourinary Cancers Symposium; Fizazi et al, NEJM 2019.



Fizazi et al, NEJM 2019

What to use in M0 CRPC?

	SPARTAN (apalutamide)	PROSPER (enzalutamide)	ARAMIS (darolutamide)
Median pre-trial PSA DT, mos	4.4	3.8	4.4
Metastasis free survival, mos	40.5 HR 0.28 (0.23-0.35)	36.6 HR 0.29 (0.24-0.35)	40.4 HR 0.41 (0.34-0.50)
Time to PSA progression, mos	NR HR 0.06 (0.05-0.08)	37.2 HR 0.07 (0.05-0.08)	33.2 HR 0.13 (0.11-0.16)
Overall survival	HR 0.70 (0.47-1.04)	HR 0.80 (0.58-1.09)	HR 0.71 (0.50-0.99)
Discontinuation rate for AE	11%	9%	9%
Grade >=3% AE	45% vs 34%	31% vs 23%	25% vs 20%

Note: Men with PSA DT of >10 months excluded from all these trials

SPARTAN, Smith et al, NEJM 2018
PROSPER, Hussain et al, NEJM 2018
ARAMIS, 2019 GU Cancers Symposium

LUNG CANCER INITIATIVE
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A NETWORK OF HOPE AND ACTION

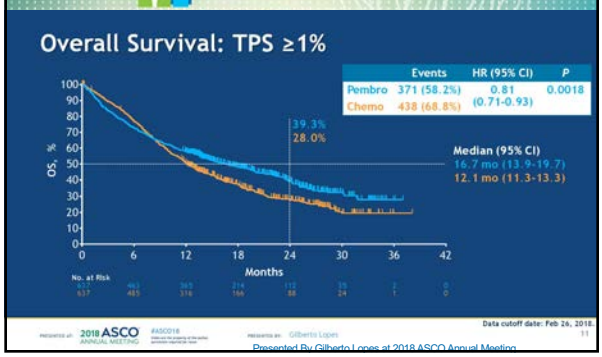
Best of ASCO Thoracic 2019, For UNCCN

Jared Weiss
Associate Professor of Medicine, UNC
Section Chief of Thoracic and Head/Neck Oncology
Board Member, LCI
VP, Cancergrace

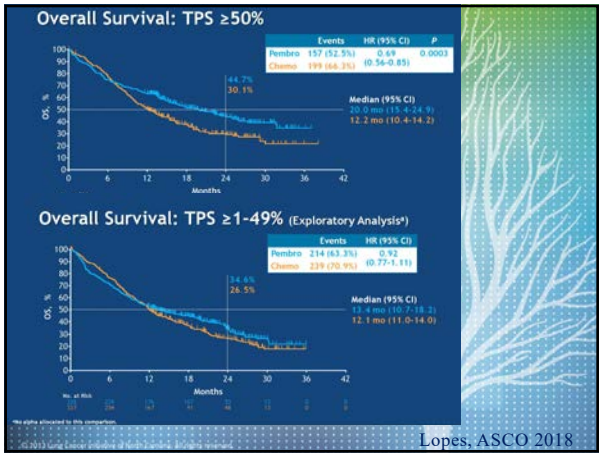
KEYNOTE-042 Study Design: Pembrolizumab vs. chemotherapy

Slide modified from Gilberto Lopes, AACR 2018

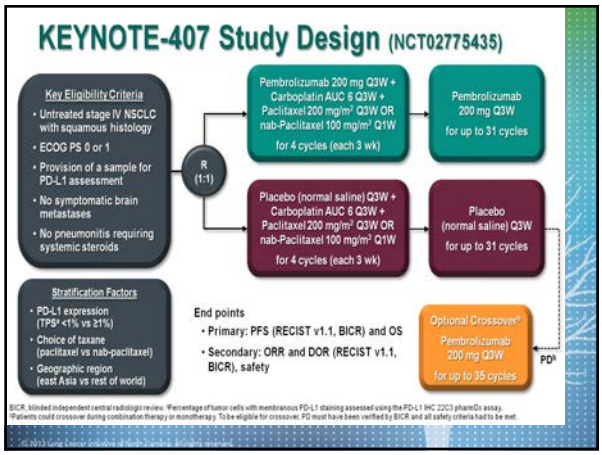
Keynote 42

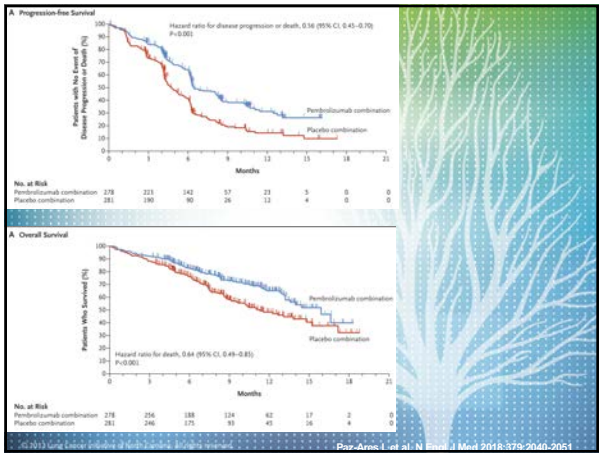


Presented By Gilberto Lopes at 2018 ASCO Annual Meeting



Lopes, ASCO 2018





Paz-Ares L et al. N Engl J Med 2018;379:2040-2051

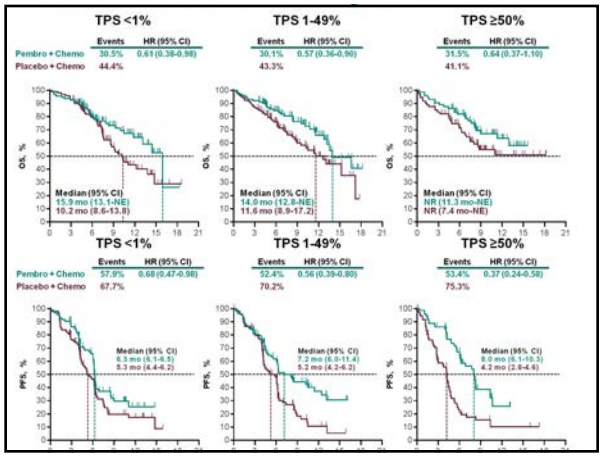
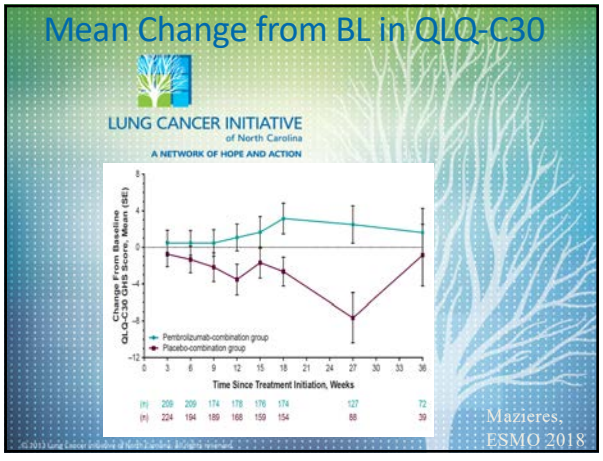
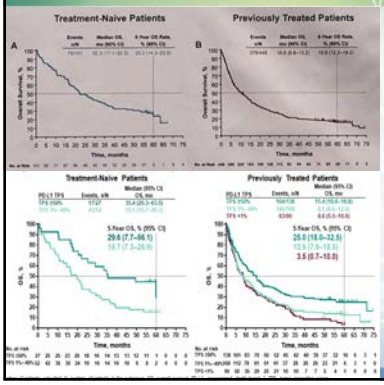


Table 3. Adverse Events of Interest in the As-Treated Population.*

Event	Pembrolizumab Combination (N=278)		Placebo Combination (N=280)	
	Any Grade	Grade 3, 4, or 5	Any Grade	Grade 3, 4, or 5
	number of patients (percent)			
Any event	80 (28.8)	30 (10.8)	24 (8.6)	9 (3.2)
Hypothyroidism	22 (7.9)	1 (0.4)	5 (1.8)	0
Hyperthyroidism	20 (7.2)	1 (0.4)	2 (0.7)	0
Pneumonitis	18 (6.5)	7 (2.5)†	6 (2.1)	3 (1.1)†
Infusion reaction	8 (2.9)	4 (1.4)	6 (2.1)	1 (0.4)
Colitis	7 (2.5)	6 (2.2)	4 (1.4)	3 (1.1)
Hepatitis	5 (1.8)	5 (1.8)	0	0
Severe skin reaction	5 (1.8)	3 (1.1)	1 (0.4)	1 (0.4)
Hypophysitis	3 (1.1)	2 (0.7)	0	0
Thyroiditis	3 (1.1)	1 (0.4)	0	0
Nephritis	2 (0.7)	2 (0.7)	2 (0.7)	2 (0.7)



Pembrolizumab @ 5 years



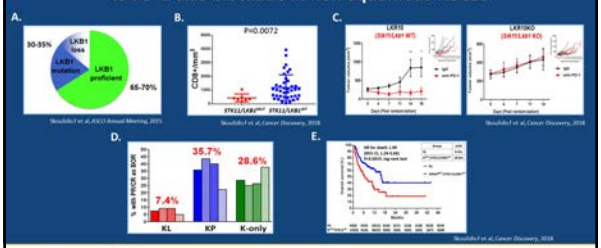
Hope, Summarized:

- 5y OS 15.5% in previously treated
- 5y OS 23.2% in 1L

Top: Garon, ASCO 2019
Bottom: Garon, Personal Comm.

Hope of Good Biomarkers, at last?

STK11/LKB1 genomic alterations are a mediator of the cold tumor immune microenvironment and a major driver of primary resistance to PD-1 axis blockade in non-squamous NSCLC



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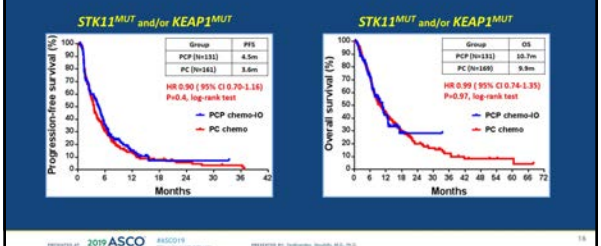
Lack of benefit from addition of pembrolizumab to CP chemotherapy in *STK11* and/or *KEAP1*-mutant non-squamous NSCLC



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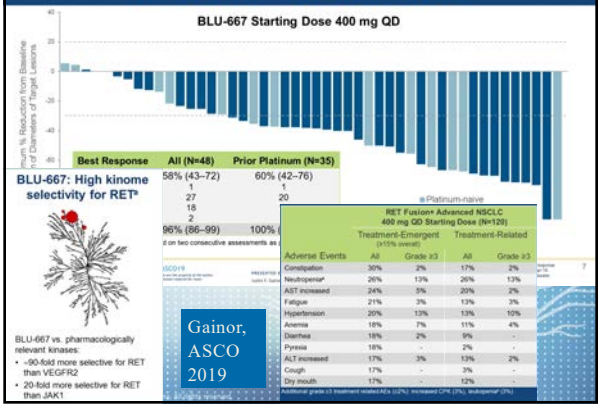
BLU-667 Demonstrates Substantial Antitumor Activity in RET Fusion+ Advanced NSCLC



Best Response	All (N=48)	Prior Platinum (N=35)
	58% (43–72)	60% (42–76)
	1	1
	27	20
	18	
	2	
	96% (86–99)	100% (

d on two consecutive assessments as

BLU-667: High kinome selectivity for RET[a]

BLU-667 vs. pharmacologically relevant kinases:
- ~90-fold more selective for RET than VEGFR2
- 20-fold more selective for RET than JAK1

RET Fusion+ Advanced NSCLC
400 mg QD Starting Dose (N=120)

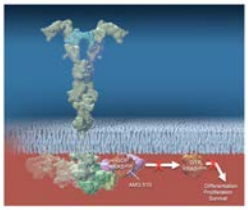
	Treatment-Emergent (≥15% overall)		Treatment-Related	
Adverse Events	All	Grade ≥3	All	Grade ≥3
Constipation	30%	2%	17%	2%
Neutropenia[a]	26%	13%	26%	13%
AST increased	24%	5%	20%	2%
Fatigue	21%	3%	13%	3%
Hypertension	20%	13%	13%	10%
Anemia	18%	7%	11%	4%
Diarrhea	18%	2%	9%	-
Pyrexia	18%	-	2%	-
ALT increased	17%	3%	13%	2%
Cough	17%	-	3%	-
Dry mouth	17%	-	12%	-

Additional grade ≥3 treatment related AEs (≥2%): increased CPK (3%), leukopenia[a] (3%)

Gainor, ASCO 2019

AMG 510 is a First in Class KRAS^{G12C} Inhibitor

- KRAS is a GTP-binding protein that links receptor tyrosine kinase activation to intracellular signaling [1,2]
- Mutation of KRAS favors the GTP-bound active state and constitutive activation of downstream effects (differentiation, proliferation, survival)[3]
- *KRAS*^{G12C} mutation has been identified as an oncogenic driver of tumorigenesis
- *KRAS*^{G12C} mutation is found in approximately 13% of lung cancer[4], 3% of colorectal (CRC)[5] and appendix cancer, and 1-3% of other solid tumors[6]
- Currently there is no approved therapy targeting this mutation
- AMG 510 is a novel, first in class, small molecule that specifically and irreversibly inhibits KRAS^{G12C} by locking it in an inactive GDP-bound state



GDP, guanosine diphosphate; GTP, guanosine triphosphate; KRAS, Kirsten rat sarcoma viral oncogene homolog; KRAS^{G12C}, KRAS protein with a G12C mutation at the protein level.

1. Prior IA, et al. Cancer Res. 2012;72:2457-2467.
2. Ostrem JM, et al. Nat Rev Drug Discov. 2016;15:771-785.
3. Ryan MB, et al. Nat Rev Clin Oncol. 2016;13:709-726.
4. Biernacka A, et al. Cancer Genet. 2016;209:195-198.
5. Cancer Genome Atlas Network. Nature. 2012;487:330-337.
6. Zhou L, et al. Med Oncol. 2014;31:43.

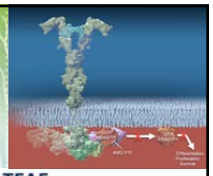
2019 ASCO ANNUAL MEETING #ASCO19

Marwan G. Fakih, MD

Presented By Marwan Fakih at 2019 ASCO Annual Meeting

AMG510

LUNG CANCER INITIATIVE of North Carolina
A NETWORK OF HOPE AND ACTION



Patient Incidence of Treatment Related TEAE

Adverse Event	Gr 1 n	Gr 2 n	Adverse Event	Gr 1 n	Gr 2 n
Diarrhea	3		Proteinuria		1
Decreased appetite	2		Dry mouth	1	
Nausea	2		Flatulence	1	
Elevated creatine phosphokinase	2		Vomiting	1	
Elevated or change in AST	1	1	Fatigue	1	
Elevated or change in ALT	1	1	WBC Decrease	1	
Elevated alkaline phosphatase	1	1	Pyrexia	1	
Cheilitis		1	Arthralgia	1	
Hyperkalemia		1	Hot flash	1	

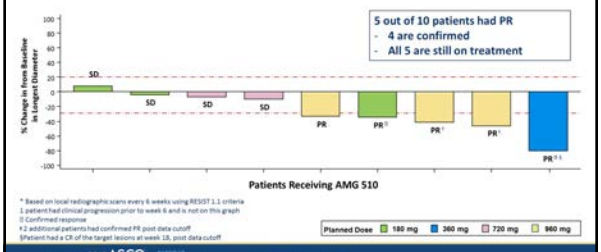
Grade 3 Adverse Event	n
Anemia[a]	1
Diarrhea[b]	1

[a]Patient had grade 2 anemia at baseline
[b]Lasting 2 days

None of the 35 patients reported:
- DLTs
- Grade 4 related AEs
- Serious related AEs

Presented By Marwan Fakih at 2019 ASCO Annual Meeting

NSCLC: Best Tumor Response* (n=10)



* Based on local radiographic scans every 6 weeks using RESIST 1.1 criteria
‡ patient had clinical progression prior to week 6 and is not on this graph
† Confirmed response
‡ 2 additional patients had confirmed PR post data cutoff
§Patient had a CR of the target lesions at week 18, post data cutoff

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EGFR Exon 20

Treatment-Related AEs in Patients Treated With TAK-788

Any grade: ≥20% of all patients Grade ≥3: ≥3% of all patients	All Patients Treated at 160 mg qd[a] (n=72)		All Patients Treated at Any Dose[b] (N=137)	
	Any Grade, %	Grade ≥3, %	Any Grade, %	Grade ≥3, %
Diarrhea	85	18	74	12
Nausea	43	6	33	4
Rash	36	1	26	1
Vomiting	29	3	22	2
Decreased appetite	25	1	22	1
Stomatitis	18	4	14	3
Increased lipase	10	6	8	3
Increased amylase	8	4	8	3

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TAK-788 Antitumor Activity in Patients With *EGFR* Exon 20 Insertions

Exon 20 Insertion Variant	No. of Patients	No. of Confirmed Responders, n	Confirmed ORR
769_ASV	5	2	40%
773_NPH	4	2	50%
Exact variant unknown	4	2	50%
Other	15	6	40%

- Median (range) best percent change: -32.5% (-100%, 26.3%)
- Three patients were excluded from the waterfall plot: 1 patient had nonmeasurable baseline target lesions, and 2 patients had no follow-up scans

IO, immuno-oncology therapy; PD, progressive disease.

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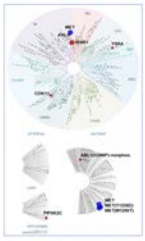
MET Del 14

Background

- *MET* exon 14 skipping mutations (*METΔex14*) are reported in 3–4% of patients with NSCLC[1-4] and associated with both poor prognosis and poor responses to standard therapies including immunotherapy.[5-9]
- Capmatinib is a highly selective *MET* inhibitor with *in vitro* and *in vivo* activity seen against preclinical cancer models with *MET* activation.[10]
- Capmatinib is the most potent inhibitor against MET compared to other inhibitors.[11]

	Capmatinib	Savolitinib	Tepotinib	Cabozantinib	Crizotinib
IC_{50} (nM)	0.6	2.1	3.0	7.8	22.5

- Preliminary efficacy data from the phase 2, multi-cohort, multicenter GEOMETRY mono-1 study showed **deep responses** with capmatinib irrespective of the line of treatment as well as **activity in the brain lesions** in patients with *METΔex14* mutated advanced NSCLC.[12]

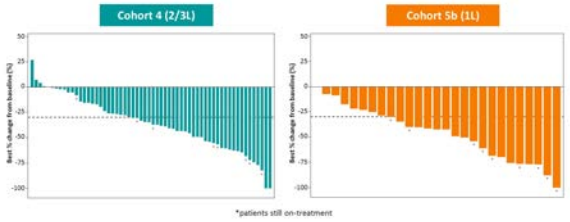


1. Gelsomino F, *et al. Cancers (Basel).* 2014;6:2100-15; 2. Ma PC. *Cancer Discov.* 2015;5:802-5; 3. Reungwetwattana T, *et al. Lung Cancer.* 2017;103:27-37; 4. Tong JH, *et al. Clin Cancer Res.* 2016;22:3048-56; 5. Dimou A, *et al. PLoS One.* 2014; 9:e107677; 6. Guo R, *et al. PLoS One.* 2014;9:e99999; 7. Saberi H, *et al. Ann Oncol.* 2018;29:2085-91; 8. Baba K, *et al. Thorac Cancer.* 2019;10:369-72; 9. Rea H, *et al. Clin Lung Cancer.* 2018;19:e441-e63; 10. Baltschukat, *et al. Clin Cancer Res.* 2019; Epub; 11. Fujino T, *et al.* WCLC 2018, Poster P1.13-41; 12. Wolf J, *et al. Ann Oncol.* 2018; 29(Suppl 8): Abstract LBA52

Capmatinib

Tumor shrinkage per BIRC

Deep responses observed in a majority of patients across both cohorts



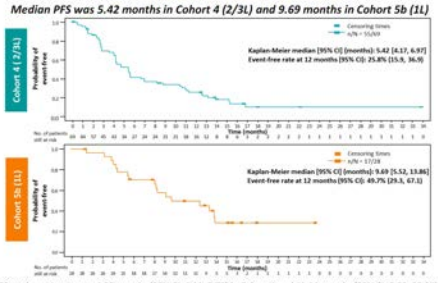
*patients still on-treatment

P

Capmatinib

Progression-free survival per BIRC

Median PFS was 5.42 months in Cohort 4 (2/3L) and 9.69 months in Cohort 5b (1L)



Median PFS per investigator was 4.80 months (95% CI: 4.11, 7.75) in Cohort 4 and 11.14 months (95% CI: 5.52, 15.24) in Cohort 5b

n is the number of events, N is the number of patients

Capmatinib

Safety summary

Favorable and manageable safety profile

Most common adverse events- treatment related (≥10%, all grades), n (%)	All Patients N = 334	
	All grades	Grade 3/4
Any	282 (84.4)	119 (35.6)
Peripheral edema	139 (41.6)	25 (7.5)
Nausea*	111 (33.2)	6 (1.8)
Increased blood creatinine†	65 (19.5)	0
Vomiting*	63 (18.9)	6 (1.8)
Fatigue	46 (13.8)	10 (3.0)
Decreased appetite*	42 (12.6)	3 (0.9)
Diarrhea	38 (11.4)	1 (0.3)

- Safety determined in the largest dataset of *MET* dysregulated‡ NSCLC patients (N=334).
- Median treatment exposure time: 14.9 weeks
- Capmatinib was well tolerated with few Grade 3/4 events [only 15 patients (4.5%) had Grade 4 events]
- Dose adjustment due to treatment related AE: 73 (21.9%)
- Discontinuation due to treatment related AE: 37 (11.1%)
  - Most frequent (≥ 1%): peripheral edema (n=6, 1.8%), pneumonitis (n= 5, 1.5%) and fatigue (n=5, 1.5%)
- Serious treatment related AEs: 43 (12.9%)

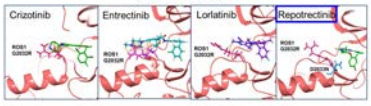
* Capmatinib administered in fasting conditions; food restriction removed in new cohorts 6 and 7
† Capmatinib is known to inhibit creatinine transporters
‡ *MET* mutated/amplified

Presented By Juergen Wolf at 2019 ASCO Annual Meeting

Targeting *ROS1* Fusion Positive Non-Small Cell Lung Cancer

- *ROS1* rearrangement is an oncogenic driver in 1-2% of NSCLC
- Crizotinib is the only approved targeted therapy for patients with advanced *ROS1*+ NSCLC
- G2032R is the most common *ROS1* resistance mutation after crizotinib treatment[1]
- **Repotrectinib is a next-generation ROS1/TRKA-C/ALK inhibitor, designed to overcome TKI resistance mutations, especially solvent front *ROS1* G2032R[2]**

Repotrectinib is a Small, Rigid Macrocycle Designed to Overcome the *ROS1* G2032R Solvent Front Mutation



CD74-ROS1 Ba/F3 Cell Proliferation IC_{50} (nM)*

ROS1	Crizotinib	Ceritinib	Cabozantinib	Entrectinib	Lorlatinib	Repotrectinib
WT	14.6	42.8	0.5	10.5	0.2	<0.2
G2032R	266.2	1391	11.3	1813	160.7	3.3

*Data based on evaluation of comparable proxy chemical reagents purchased from commercial sources except repotrectinib

[1]Gainor JF et al., JCO Precis Oncol 2017
[2]Drilon A et al., Cancer Discov 2018

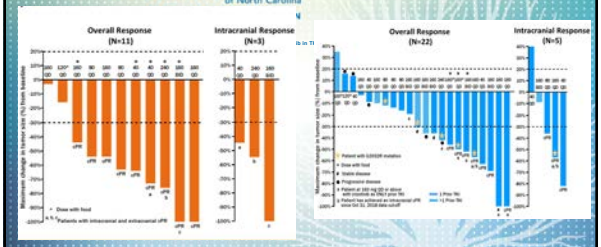
PRESENTED AT: 2019 ASCO ANNUAL MEETING #ASCO19 PRESENTED BY: B.C. Cho, M.D., Ph.D.

Presented By Byoung Chul Cho at 2019 ASCO Annual Meeting

Repotrectinib in TKI Naïve ROS1+ NSCLC

Repotrectinib in TKI Pretreated ROS1+ NSCLC

LUNG CANCER INITIATIVE of North Carolina



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Future Oncologists

LUNG CANCER INITIATIVE of North Carolina