

Testing for Molecular Markers and Sequencing of Treatments in Advanced NSCLC Ex-Smoker with an Adenocarcinoma



Dr. Thomas Hensing
Medical Oncologist
Co-Director,
Thoracic Oncology Program
Northshore Univ. HealthSystem
Chicago, IL



Dr. David Jackman
Medical Oncologist
Instructor in Medicine
Harvard Medical School
Dana Farber Cancer Institute
Boston, MA



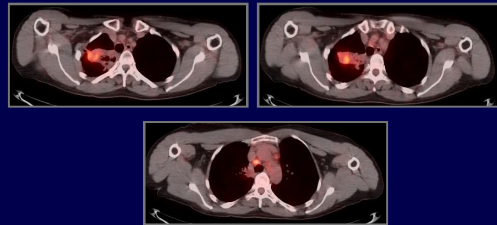
with Howard (Jack) West, MD
Medical Oncologist
President & CEO
GRACE

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Stage IVa Adeno NSCLC, Background

- 51 yo ex-smoker (1/2 ppd x 25 years, quit 1999) without much medical history, apparent locally advanced NSCLC
- Pain in right upper chest, initially felt related to crash while sledding 12/09, but didn't improve
- PCP ordered CXR: RUL mass
- CT C/A/P: R apical mass 3.6 x 2.3 x 4.2 cm, mildly enlarged nodes AP window, no evidence of distant disease
- Bronch/EBUS: FNA R pretracheal node: NSCLC (NOS)
- Referred to thoracic surgeon, mediastinoscopy: adenoCa in mult stations: 2R, 4R, station 7, L paratracheal
- Referred to med onc, rad onc for chemo/radiation

Imaging, 51 yo woman with Adeno NSCLC



Stage IVa Adeno NSCLC, Background (cont.)

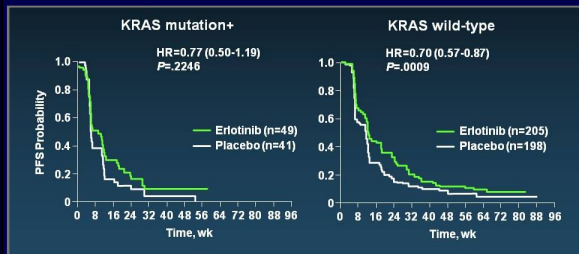
- Works as administrator in local school system
- No PMH, excellent performance status
- New R pleural effusion on planning CT
– thoracentesis positive for NSCLC
- Relatively young, good performance status, moderate smoking history (not within usual range of "oligo-smoker"), with stage IVa NSCLC, adenocarcinoma histology

Would you be inclined to send for molecular markers prior to starting treatment? Which ones?

Presume *ALK* rearrangement isn't available immediately. If *EGFR* and *KRAS* wild type, would you send for *ALK* rearrangement? If yes, would you wait on starting therapy?

How does *KRAS* affect your clinical decision making, whether for first line or later therapy?

SATURN: Progression-Free Survival According to *KRAS* Mutations

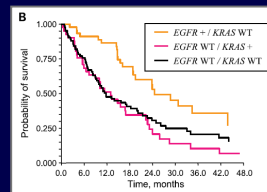


Brugger, ASCO 2009

Clinical Cancer Research, 2009

Impact of Epidermal Growth Factor Receptor and *KRAS* Mutations on Clinical Outcomes in Previously Untreated Non-Small Cell Lung Cancer Patients: Results of an Online Tumor Registry of Clinical Trials

David M. Jackman,^{1,2} Vincent A. Miller,⁴ Leigh-Anne Cioffredi,¹ Beow Y. Yeap,^{2,3} Pasi A. Jänne,^{1,2} Gregory J. Riely,⁴ Marielle Gallegos Ruiz,⁵ Giuseppe Giaccone,⁶ Leticia V. Sequist,⁷ and Bruce E. Johnson^{1,2}



	EGFR + / KRAS WT	EGFR WT / KRAS +	EGFR WT / KRAS WT	P
N	47	41	83	
RR	68%	0	5%	< .001
Median TTP (months)	13.1	3.3	3.1	< .0001
Median OS	24.5	13.0	11.8	.002

Having a *KRAS* mutation does not mean that a person with advanced NSCLC shouldn't receive an EGFR inhibitor as treatment at some point?

Because they appear to be nearly mutually exclusive findings, would detecting an *EGFR* or *KRAS* mutation lead you to **not** test for an *ALK* rearrangement?

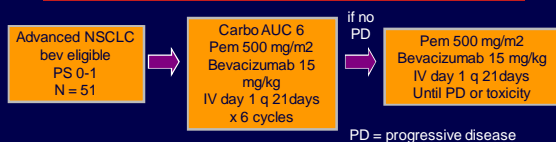
First Line Treatment

- She starts carboplatin/pemetrexed with bevacizumab and tolerates it very well, with no significant adverse effects.
- After two cycles, she demonstrates partial response, and then stable disease after four cycles.
- Performance status remains excellent.

When would you be inclined to change her treatment?

Would you recommend continuation maintenance, switch maintenance, or observation?

Carbo/Alimta/Avastin → Maintenance Alimta/Avastin in Eligible Patients with Advanced NSCLC

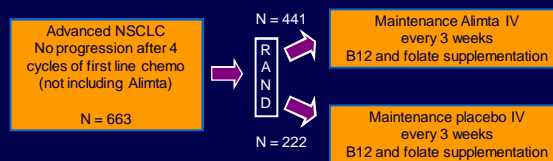


- Up to 31 cycles administered, median 6
- 30 patients completed 6 or more cycles of chemo/bev
- No grade ≥ 3 bleeding, very mild heme toxicity, 8% grade 3 fatigue, a few with diverticulitis (?why)
- ORR 49%
- Med TTP 7.2 months
- Med OS 14.0 months

Patel, J Clin Oncol 2009

JMEN: Maintenance Alimta (Pemetrexed) vs. Placebo after First-Line Chemotherapy

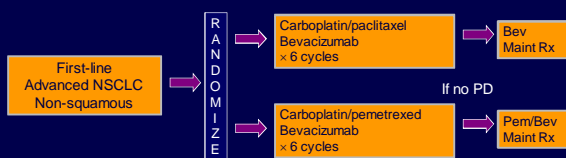
- Does going on maintenance Alimta after four cycles of first-line chemo improve progression-free survival (PFS)?



Ciuleanu, Lancet 2009

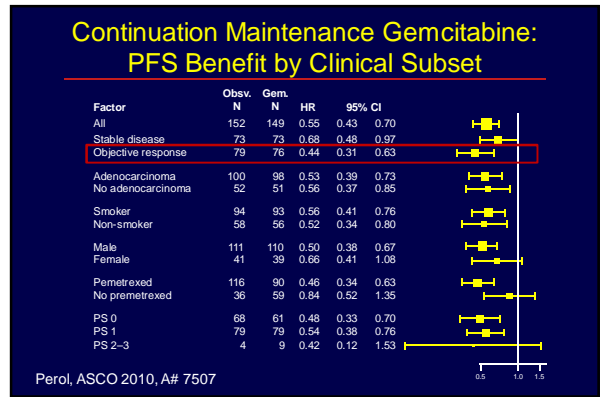
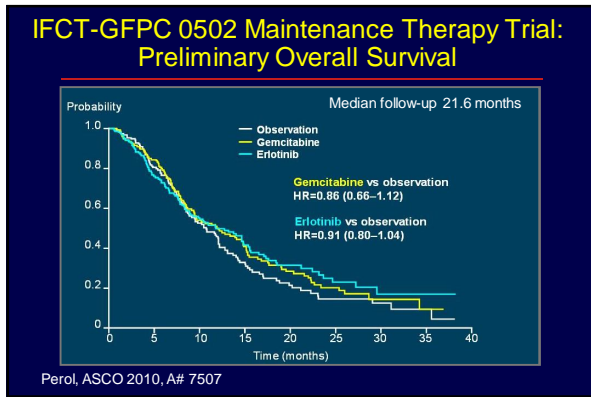
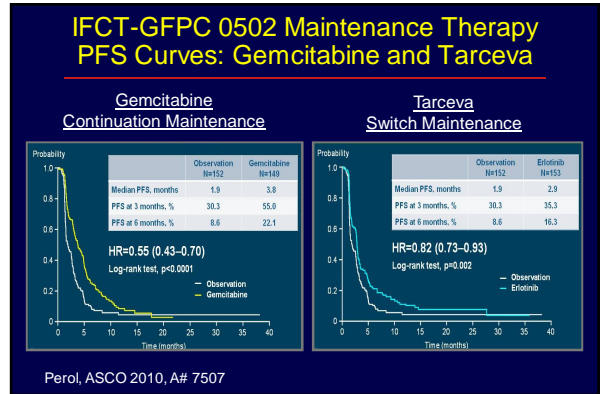
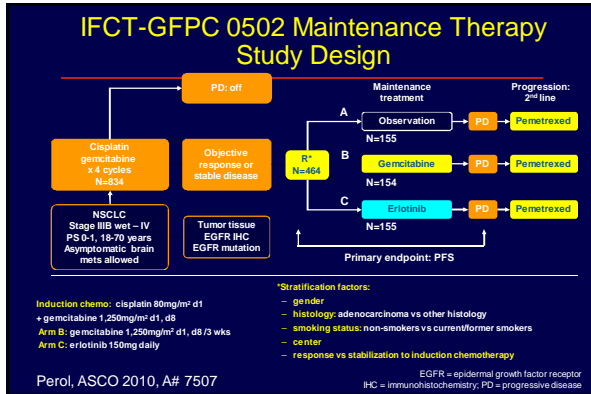
“POINT BREAK” Trial: ECOG 4599 vs. ABC/ “Patel” Regimen

Primary investigator: Dr. Jyoti Patel, Northwestern



Primary endpoint: Survival

Is stopping treatment after 4-6 cycles of first line chemotherapy potentially discontinuing a treatment before exhausting its benefit?



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