Targeted therapy for BRAF-mutant lung cancer: results from the European EURAF cohort study

Gautschi O, Bluthgen MV, Smit EF, Wolf J, Früh M, Peters S, Schuler M, Zalcman G, Milia J, Mazières J; on behalf of the EURAF collaborators.

elcc

15-18 April 2015, Geneva, Switzerland

Organisers IASLC International Association for the Study of Lung Cancer; ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE European Society for Medical Oncology

Partners ESTRO European Society for RADIOTHERAPY & ONCOLOGY; European Society of Thoracic Surgeons 1993; etop Information | Research

Disclosures

- MS received honoraria from GSK and Novartis for advisory boards
- All other authors declared no relevant conflicts of interest

Background

- BRAF mutations are oncogenic drivers in 1-3% of lung carcinomas[1,2]
- Vemurafenib induced responses in individual pts[3,4]. In VE-BASKET, ORR was 42% (n=19)[5]
- Dabrafenib showed ORR of 32% and PFS of 5.5months in the BRF113928 trial[6]

(1) Paik JCO 2011; (2) Marchetti JCO 2011; (3) Gautschi JTO 2012; (4) Peters JCO 2013; (5) Hyman ASCO 2014; (6) Planchard ESMO 2014

Aims and patient selection

- Study the characteristics and clinical histories of patients with BRAF-mutant NSCLC and BRAF targeted therapy outside of a clinical trial
- Calculate ORR, PFS and OS
- Develop further collaborative trials for specific patient populations

Methods

- Retrospective study with contributors of the previous EUROS1 and EUHER2 cohorts[1,2]
- Local BRAF testing and targeted therapy
- Local response assessment by RECIST1.1
- Registration by Dec 31, 2014 (abstract)
- **Update by Feb 28, 2015 (oral presentation)**

(1) Mazières JCO 2013; (2) Mazières JCO 2015

Patient characteristics

Sample size (N)	**35**
Age at diagnosis	
- Median years (range)	63 (42-85)
Gender	
- Male	18 (51%)
- Female	17 (49%)
Smoking status	
- Never	14 (40%)
- Former/current	16 (46%)
- Unknown	5 (14%)
Country	
- France	13 (37%)
- Switzerland	10 (28%)
- Germany	7 (20%)
- The Netherlands	4 (11%)
- Austria	1 (3%)
Systemic therapy	
- Median lines (range)	3 (1-6)
- Platin based frontline therapy	30 (86%)

Tumor characteristics

Sample size (N)	**35**
NSCLC histology	
- Adenocarcinoma	35 (100%)
- Other	0
Stage at initial NSCLC diagnosis	
- I-II	1 (3%)
- III	4 (11%)
- IV	30 (86%)
Metastatic sites of special interest	
- Malignant effusion	10 (29%)
- Brain metastases	6 (17%)
BRAF mutation	
- V600E	29 (83%)
- Non-V600E	6 (17%) : G466V, G469A, G469L, G596V, V600K, K601E
Other driver mutations	
- No	34 (97%)
- Yes	1 (3%) : KRAS V12 with BRAF V600K

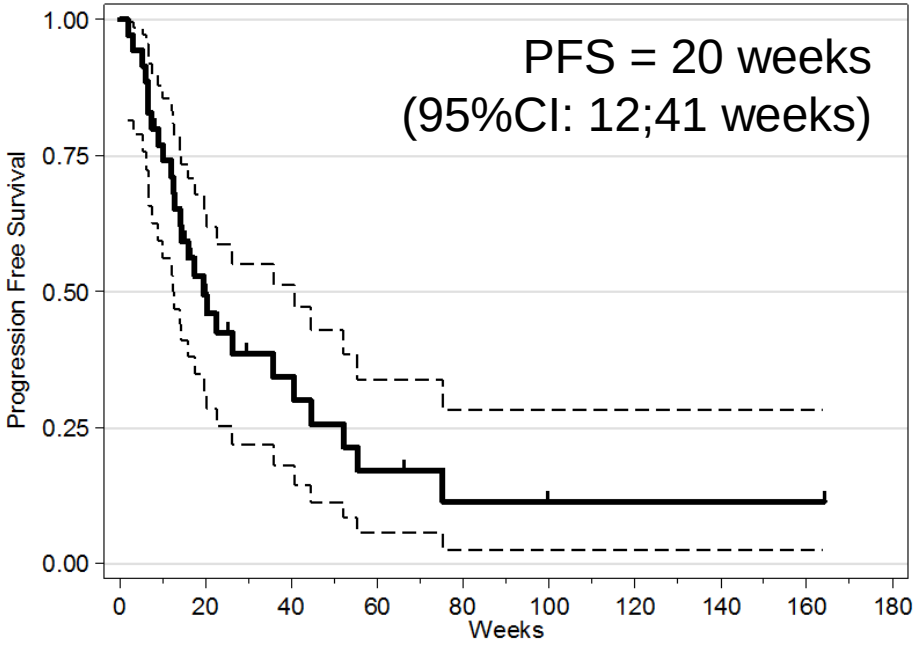
Drug exposure

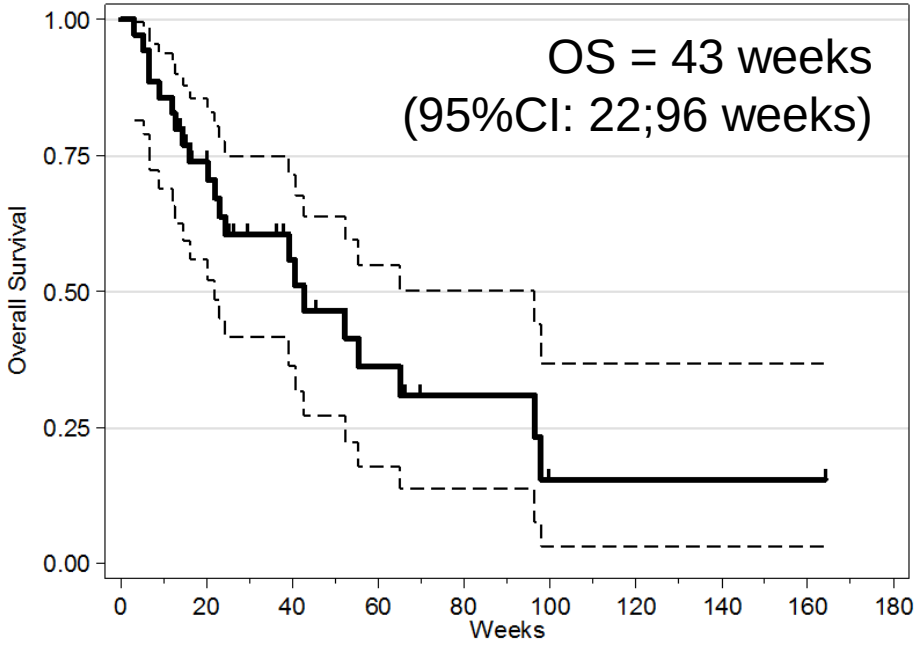
Sample size (N)	**35**
BRAF inhibitor therapy	35 (100%)
BRAF inhibitors and lines (total) - Vemurafenib - Dabrafenib - Sorafenib	39 29 9 1
Sequential BRAF inhibitors - No - Yes	 31 (89%) 4 (11%) : 3x V->D and 1x S->V
BRAF inhibitor used in - First line - Further lines	 5 (14%) 30 (86%)

Best response with BRAF therapy

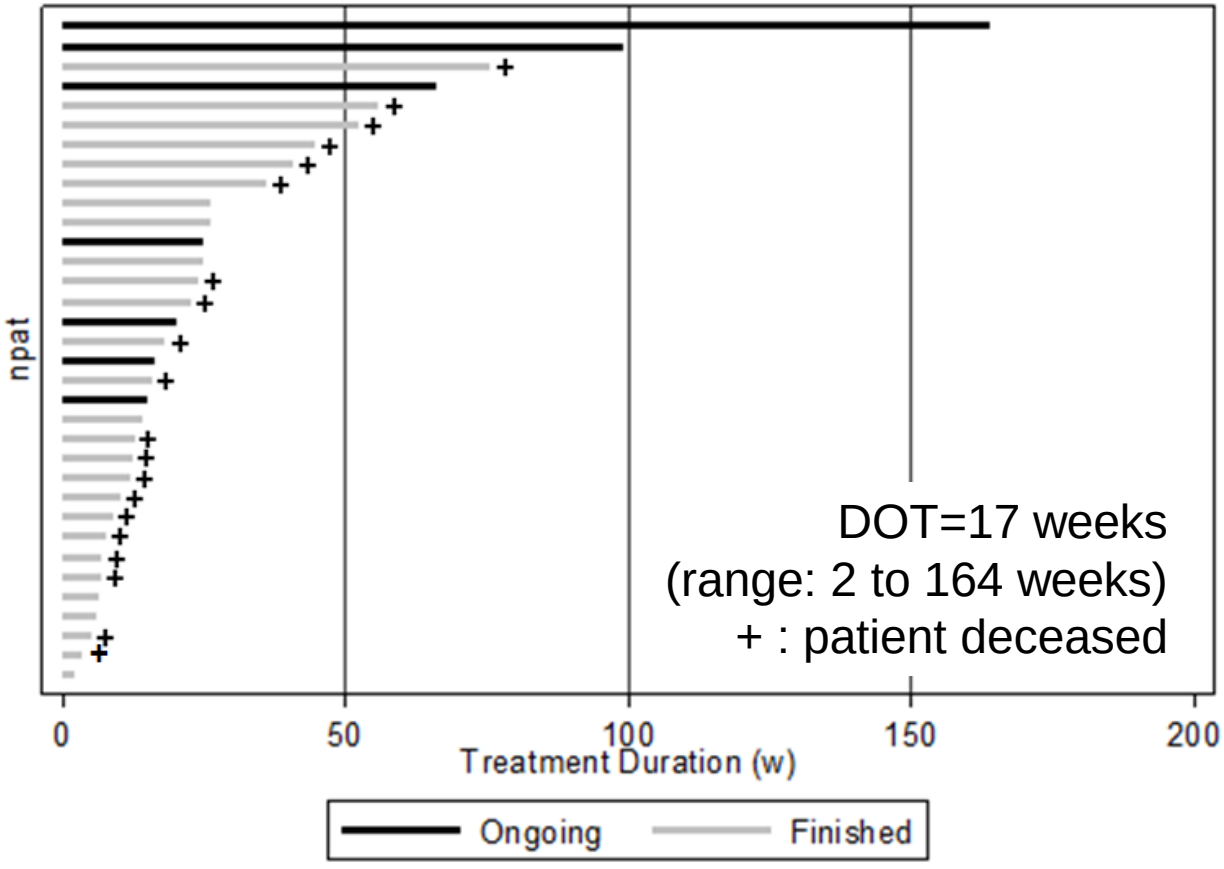
	All patients (N=35)	V600E and vemurafenib subgroup (N=25)
Data missing	1	1
- Not evaluable	1 (3%)	1 (4%)
- CR	2 (6%)	2 (8%)
- PR	16 (47%)	11 (46%)
- SD	11 (32%)	10 (42%)
- PD	4 (12%)	0
ORR	**18 (53%)** [95%CI: 35;70]	**13 (54%)** [95%CI: 33;74]
DCR	**29 (85%)** [95%CI: 69;95]	**23 (96%)** [95%CI: 79;100]

Survival with BRAF therapy

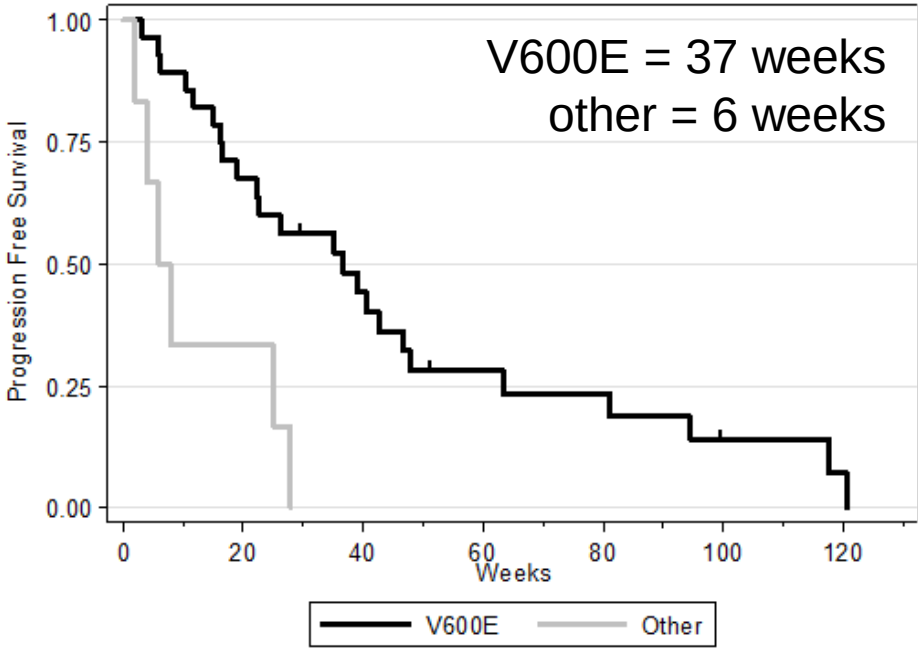


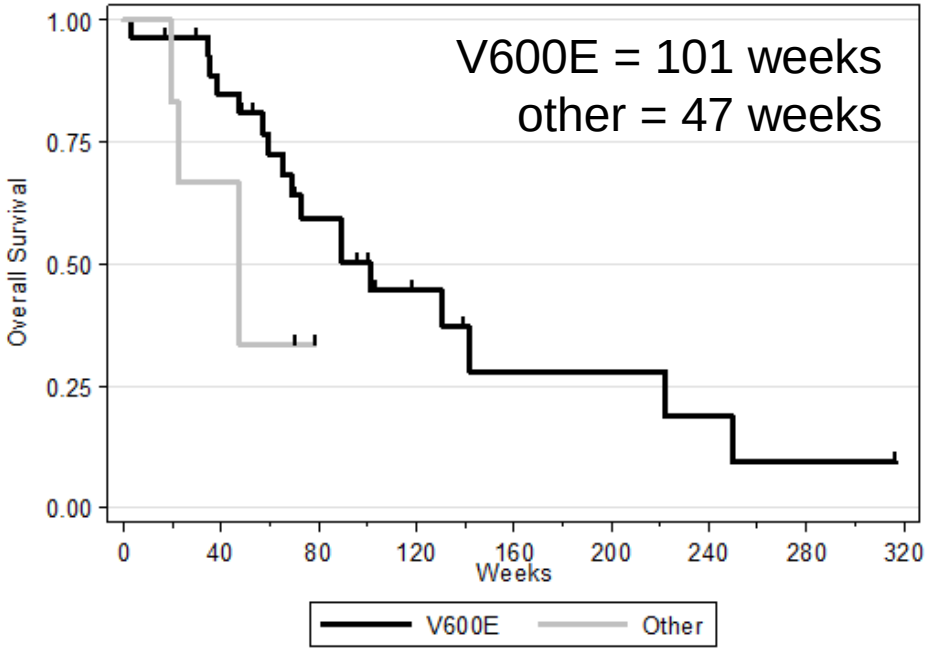


Duration of BRAF therapy



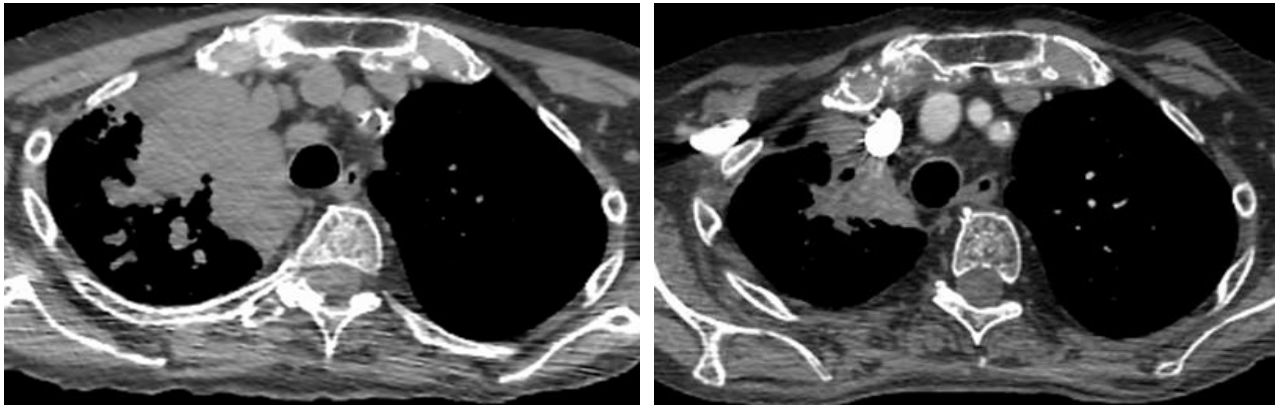
Survival from first line therapy



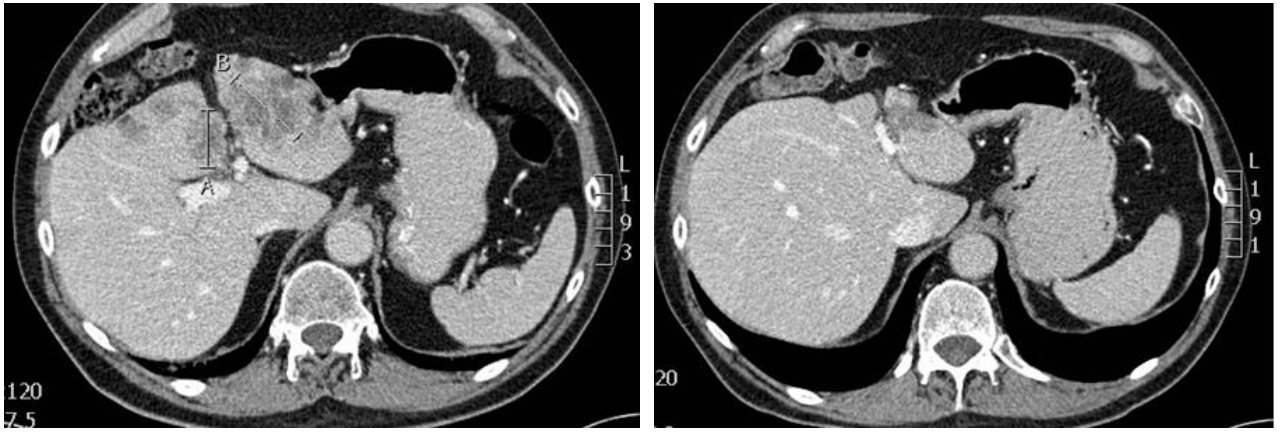


Exceptional responders

Rapid remission with vemurafenib in BRAF V600E
(J. Mazières, F)



Rapid remission with vemurafenib in BRAF V600E
(D. Koeberle, CH)



Futher observations

- Remissions were seen in 3/5 firstline BRAFi, with rechallenge[1], and in G596V
- No remissions were seen of brain metastases, and in the KRAS/BRAF-double mutant
- Chemotherapy activity was as expected, no remissions were seen with erlotinib

(1) Schmid Lung Cancer 2015

Conclusions

- Activity of BRAF inhibitors in BRAF-mutant lung cancer was confirmed
- Responders included patients with advanced age, heavy pretreatment, and poor PS
- PFS was consistent with the dabrafenib trial[1]
- Combination trials are ongoing or planned

(1) Planchard ESMO 2014

Acknowledgment

- **Study coordinator:** *Milia J*
- **Statistical analysis:** *Cabarrou B, Filleron T*
- **EURAF contributors:** *Besse B, Bluthgen MV, Burmeister H, Cappuzzo F, Curioni A, Dansin E, Diebold J, Dingemans AMC, Fournel P, Früh M, Gautschi O, Huret B, Karachaliou N, Koeberle D, Léna H, Mazières J, Michels S, Molina A, Monnet I, Mouzaoui A, Oulkhouir Y, Pall G, Peters S, Quoix E, Rosell R, Rothschild S, Scheffler M, Schmid-Bindert G, Schuler M, Smit EF, Thiberville L, Veillon R, Wannesson L, Wolf J, Zalcman G.*