Final report on the ETAP trial (PPSHP 55/2013, EudraCT 2013-002049-13, ML29075)

ETAP trial was an investigator initiated, randomized phase 2 trial investigating use erlotinib in combination with chemotherapy compared (experimental) to chemotherapy (comparator) alone in *EGFR* mutant or EGFR TKI benefitting patients with stage IIIB/IV NSCLC. The trial was approved by EC 12.08.2013 and medicinal agencies (FIMEA) 29.11.2013 after which patient recruitment was initiated. Anticipated study population was 80 and the actual recruitment was 18 (Table 1). Patient demographics did not differ markedly between the experimental and comparator arms (Table 2).

Table 1 Patient recruitement

Center	Code	Number of patients	1st patient recruited	Last patient visit
Oulu University Hospital	001	6	04.02.2014	05.07.2016
Helsinki University Hospital	002	6	07.03.2014	18.10.2016
Tampere University Hospital	003	1	10.10.2014	22.10.2014
Turku University Hospital	004	2	04.03.2015	17.03.2016
Kuopio University Hospital	007	3	17.03.2015	31.10.2016

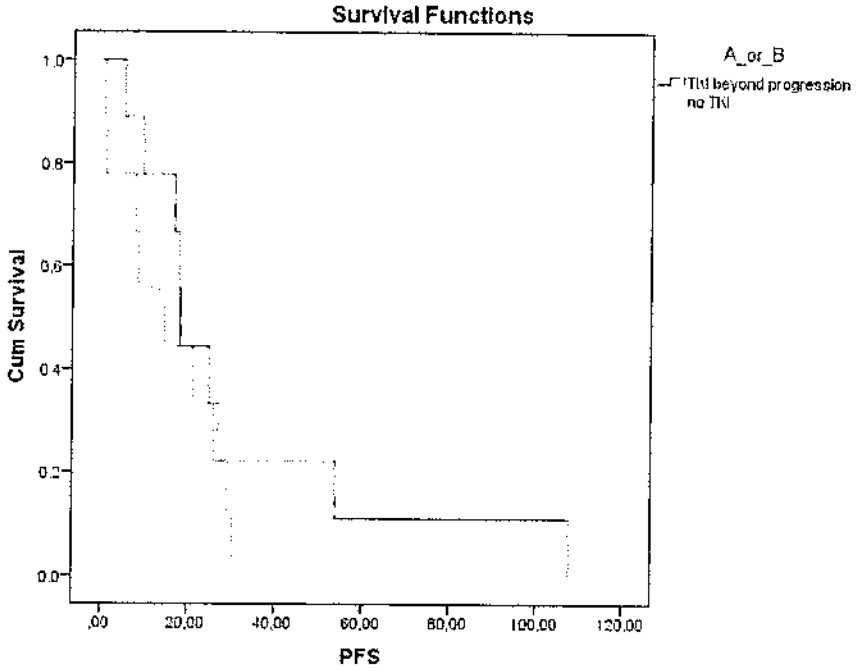
Table 2 Patient demographics

	Chemotherapy (%)	Chemotherapy+Erlotinib (%)	sig
Gender (female)	7 (79)	4 (44)	NS
Never smoker	4 (44)	4 (44)	NS
Mutation			NS
ex19del	8 (89)	5 (56)	
L858R	1 (11)	3 (33)	
G719X	0 (0)	1 (11)	
Initial stage IV/IIB	9 (100)	6 (67)	NS
ECOG			
0-1	8 (89)	6 (67)	NS
2	1 (11)	3 (33)	
Previous TKI			NS
Erlotinib	6 (67)	4 (44)	
Gefitinib	2 (22)	4 (44)	
Other	1 (11)	0 (0)	
Multiple TKIs	0 (0)	1 (11)	
TKI response			NS
PR	9 (100)	8 (89)	
SD	0 (0)	1 (11)	

Efficacy measures

The primary endpoint of the study was PFS in which study was unable to show additional benefit of combining erlotinib to chemotherapy (Figure 1). Furthermore, ORR (Table 3) or OS didn't show additional benefit of experimental therapy. However, it is worth mentioning that in there was tendency for better for the experimental treatment both in the PFS and OS survival curves (Figure 1).

Figure 1 PFS (wks, p=0.305) and OS (wks, p=0.341) for TKI beyond progression (experimental) and no TKI (comparator) according to treatment arm.



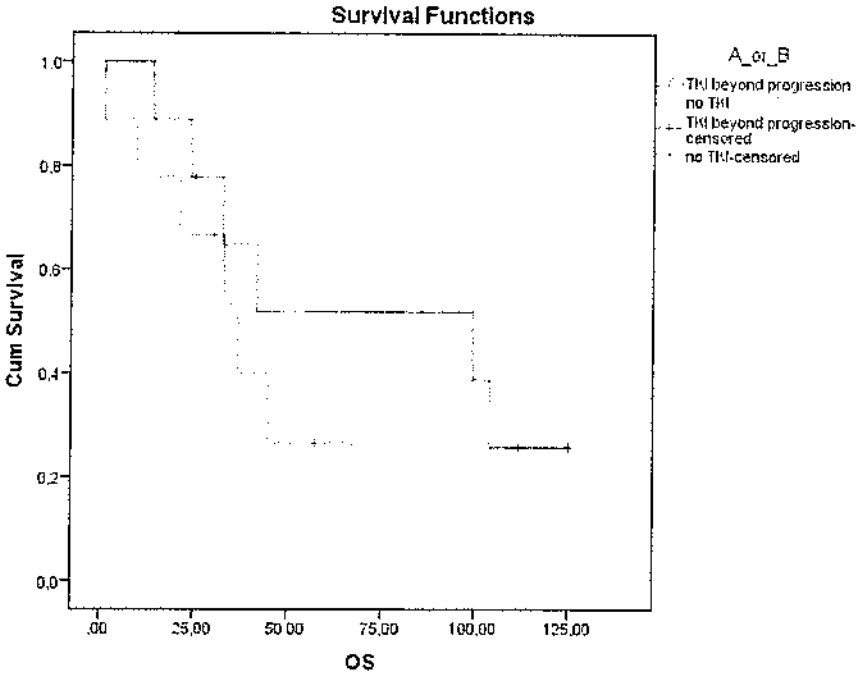


Table 3 ORR according to treatment arm

Response	Chemotherapy (%)	Chemotherpy+Erlotinib (%)	sig
CR	0 (0)	0 (0)	NS
PR	2 (25)	1 (11)	
SD	3 (38)	5 (56)	
PD	3 (33)	3 (33)	

Safety measures

61% of the patients in the study experienced gr3-4 NCI-CTCAE adverse events (AE) which were assessed to be related to study medication. Most common related gr3-4 AEs was neutropenia/neutropenic fever which occurred in 33% of the patients while there were no other gr3-4 AE occurred more than on a single patient. 33% of the patients were hospitalized during study. There was one death during study (comparator arm) which was thought be unrelated to study medication. There was no difference in gr3-4 AEs, hospitalization or death during study between the treatment arms (Table 4).

Table 4 Safety measures according to treatment arm

	Chemotherapy (%)	Chemotherapy+Erlotinib (%)	sig
Gr3-4 (related)	6 (67)	5 (56)	NS
Neutropenia/neutropenic fever	4 (44)	2 (22)	
Hospitalization	2 (25)	4 (50)	NS
Death during study			NS
Related	0 (0)	0 (0)	
Non-related	1 (13)	0 (0)	

Oulu 21st, Jun, 2017,

Jussi Koivunen, M.D., Ph.D

Study Sponsor

Dept of Oncology and Radiotherapy

Oulu University Hospital, Oulu, Finland

Mail: PB20, 90029 OYS, Finland

Email: jussi.koivunen@ppshp.fi

Tel: +35883153789