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AFATINIB FOLLOWED BY OSIMERTINIB IN REAL-WORLD PATIENTS WITH *EGFR* MUTATION-POSITIVE NSCLC: AN OBSERVATIONAL STUDY

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Disclosures

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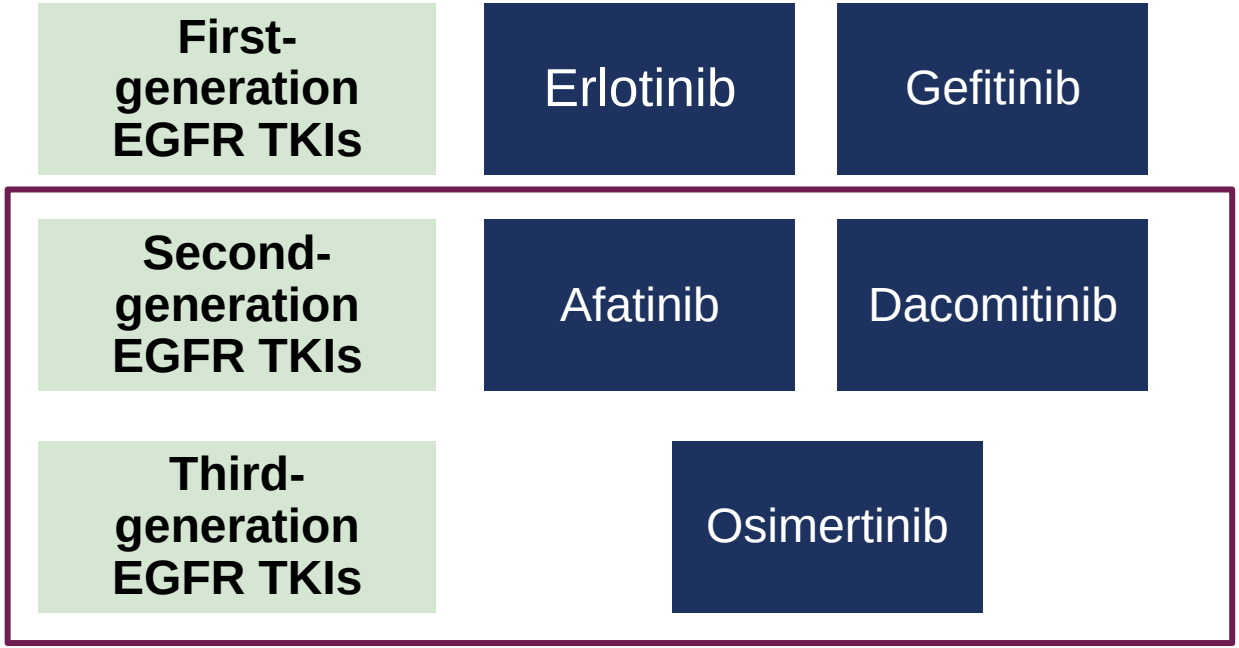
EGFR mutation-positive NSCLC: choice of first-line treatments



TKI, tyrosine kinase inhibitor

Choice of treatment strategy: availability of subsequent treatment options is a key consideration

- Regardless of which first-line TKI is chosen, acquired resistance is inevitable
- Emergence of the T790M mutation is the main molecular resistance mechanism to gefitinib, erlotinib and afatinib (present in ~50–70% of tumors at the time of acquired resistance)
- Osimertinib is the only globally approved T790M inhibitor
- Treatment with sequential EGFR TKIs, with osimertinib reserved as a second-line option, may therefore maximize time on targeted drugs

GioTag study

The first global, observational study to evaluate outcomes of patients who received first-line afatinib followed by osimertinib (NCT03370770)

- Medical and electronic health records of consecutive patients treated in a real-world practice were retrospectively reviewed
- Patients with *EGFR*-mutated (Del19/L858R) TKI-naïve advanced NSCLC who were treated first-line with afatinib, developed T790M, and received second-line osimertinib treatment
- **Primary outcome:** time on treatment

GioTag study: inclusion criteria

Medical and electronic health records of consecutive patients who met the following criteria were retrospectively reviewed between December 28, 2017 and May 31, 2018

- Had *EGFR*-mutated (Del19/L858R) TKI-naïve advanced NSCLC, were treated first-line with afatinib, developed the T790M mutation and received second-line osimertinib treatment
- Aged ≥18 years
- Provided written informed consent where required
- Patients could have received osimertinib as part of a compassionate use or expanded access program
- Inclusion was restricted to patients who initiated osimertinib treatment ≥10 months prior to enrollment to avoid early censoring and ensure mature data
- A maximum of 15 patients were enrolled per site

Patients were excluded if they had:

- Received any other first- or second-line treatments
- Active brain metastases at the start of either afatinib or osimertinib therapy
- Been treated within a clinical trial

GioTag: 204 patients across 10 countries

204 patients (Austria, Canada, Israel, Italy, Japan, Singapore, Slovenia, Spain, Taiwan and the United States) received first-line afatinib

Patients discontinued due to:

- Progressive disease (n=190)
- AE/ADR (n=10)
- Other/no data (n=4)

All 204 patients acquired the T790M mutation and received second-line osimertinib

At the time of the analysis, 106 patients had discontinued osimertinib, due to:

- Progressive disease (n=98)
- AE/ADR (n=2)
- Death (n=4)

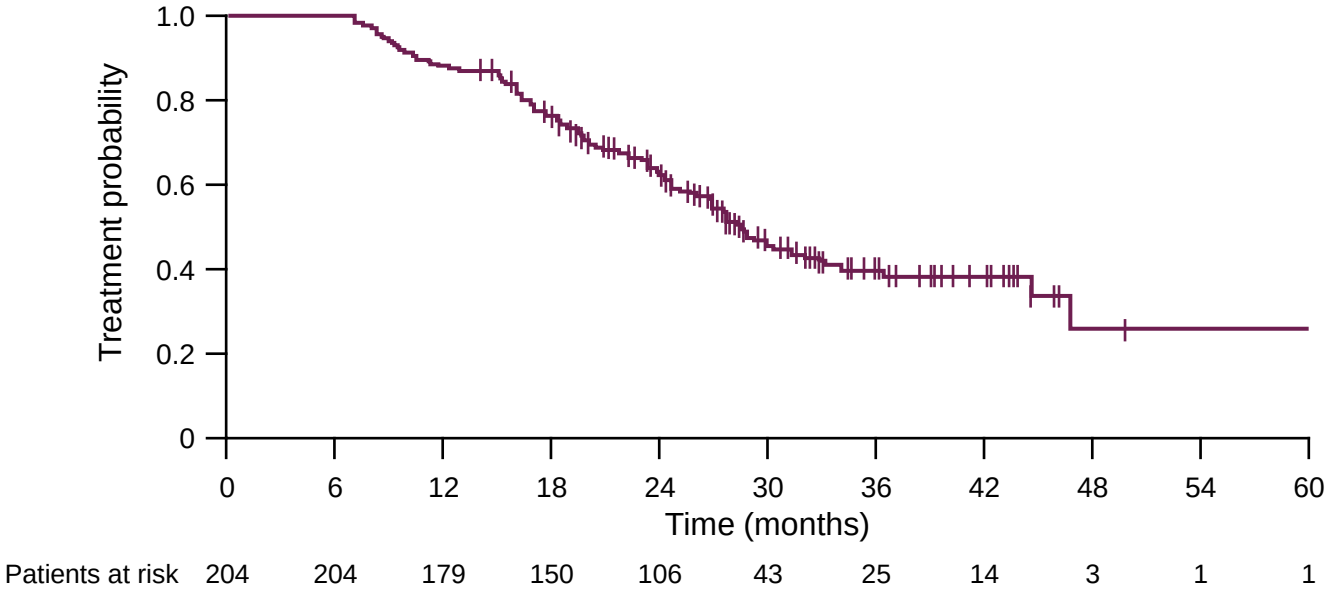
ADR, adverse drug reaction; AE, adverse event

Patient characteristics were typical of a first-line *EGFR*m+ NSCLC population

	At start of afatinib therapy
Female, n (%)	110 (53.9)
Median age, years (range)	60.0 (30–86)
Median weight, kg (range)	70.2 (37–116)
Median BMI, kg/m^2 (range)	25.3 (15.0–45.2)
Ethnicity, n (%)	
Asian	50 (24.5)
Non-Asian	138 (67.6)
Stage IV disease, n (%)	197 (96.6)
EGFR mutation, n (%)	
Del19	150 (73.5)
L858R	53 (26.0)
Del19 + L858R	1 (0.5)
ECOG PS 0 / 1 / ≥2, n (%)	43 (21.1) / 110 (53.9) / 31 (15.2)
Presence of brain metastases, n (%)	21 (10.3)

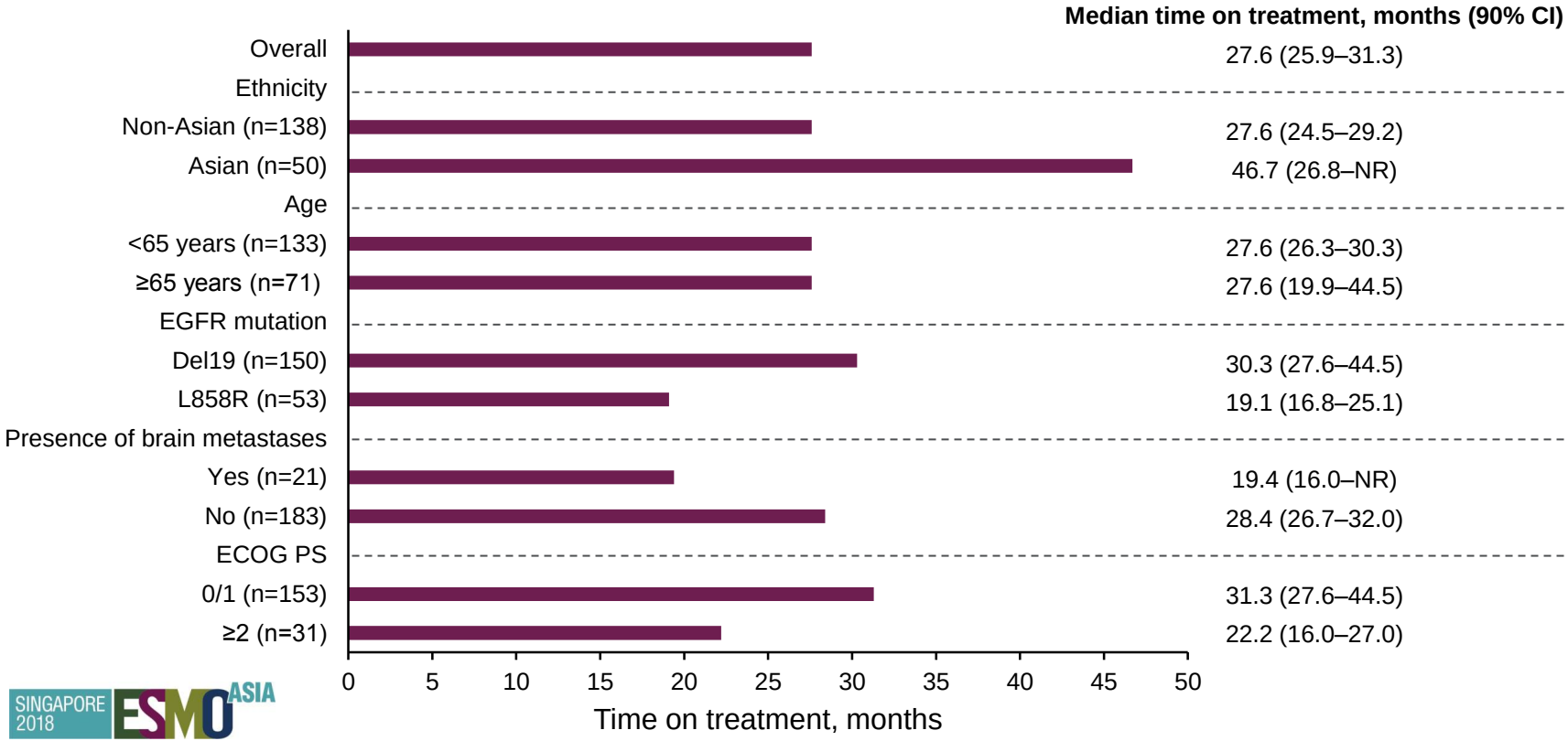
ECOG PS, Eastern Cooperative Oncology Group performance status

Sequential afatinib and osimertinib provided sustained clinical benefit in real-world clinical practice

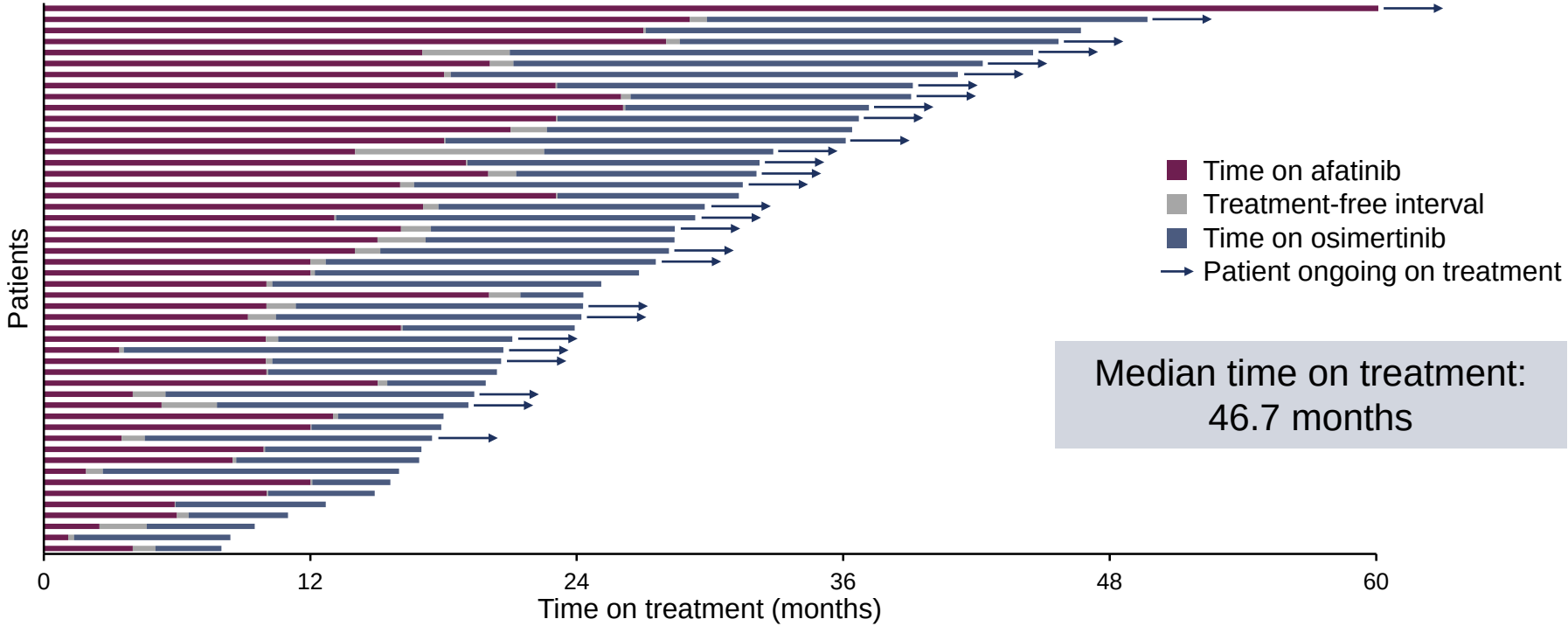


Overall median time on treatment: 27.6 months (90% CI: 25.9–31.3)

Clinical benefit of sequential treatment was seen across patient subgroups



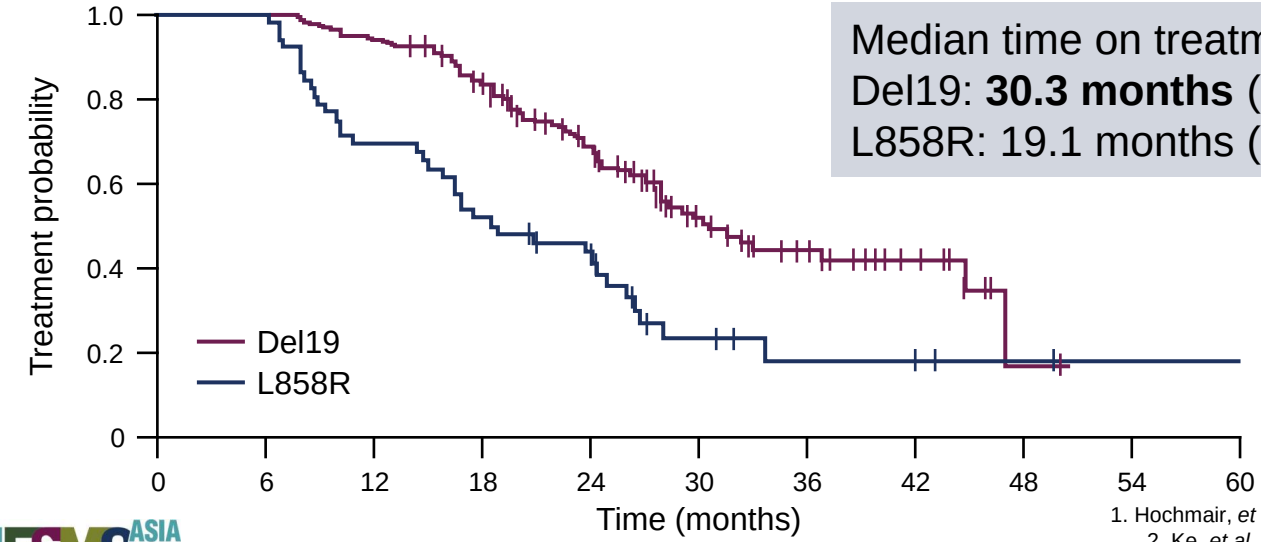
Prolonged treatment duration in Asian patients



Median time on treatment:
46.7 months

Prolonged benefit in patients with Del19-positive disease

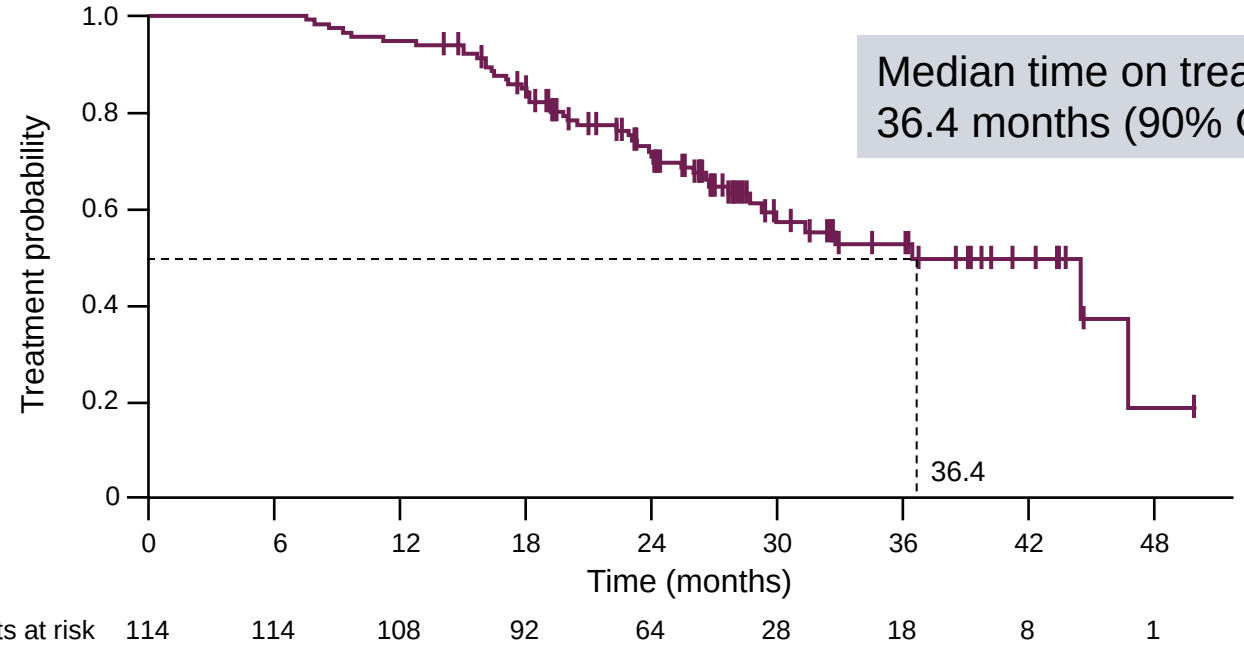
- Approximately 75% of patients had Del19-positive disease
- This high proportion likely reflects the higher frequency of T790M acquired resistance in Del19-positive versus L858R-positive tumors
  - ~75% of patients with Del19-positive disease may acquire T790M resistance[1-4]



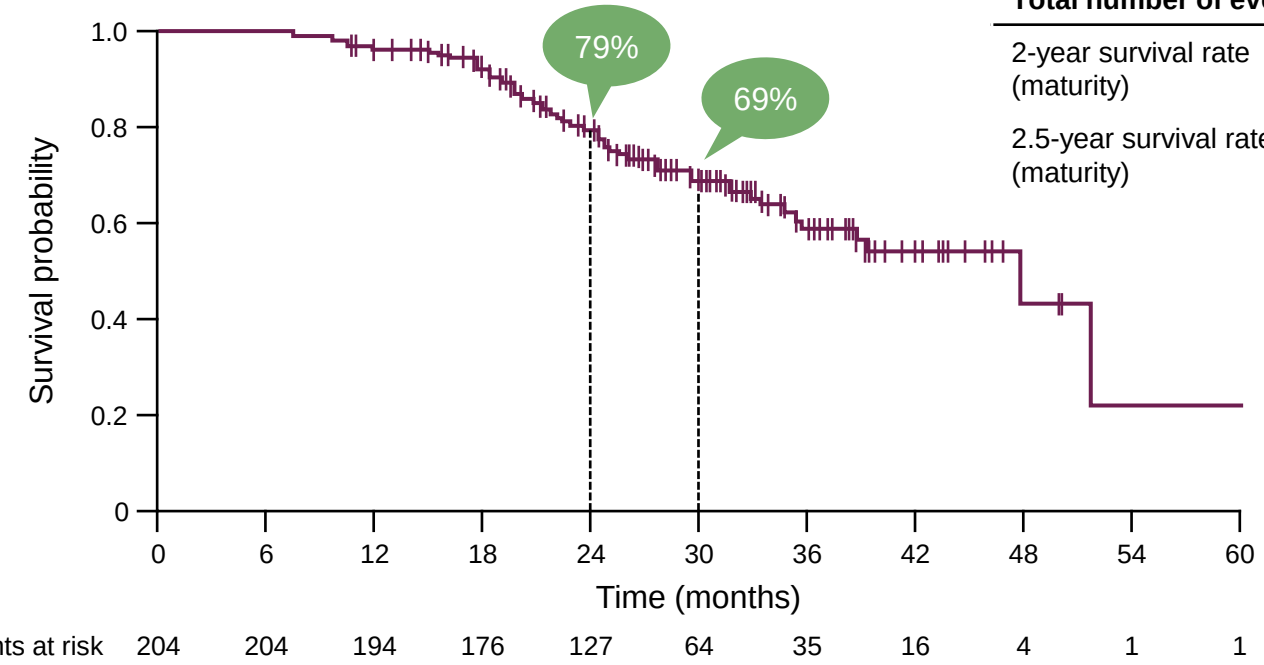
Median time on treatment
Del19: **30.3 months** (90% CI: 27.6–44.5)
L858R: 19.1 months (90% CI: 16.8–25.1)

1. Hochmair, *et al. J Thorac Oncol*. 12(11), S2137 (2017)
2. Ke, *et al. J Thorac Oncol*. 12(9), 1368-1375 (2017)
3. Matsuo, *et al. Sci Rep*. 6(1), 36458 (2016)
4. Wu, *et al. Oncotarget*. 7(11), 12404-12413 (2016)

Benefit was particularly notable in Del19 patients with ECOG PS 0/1



Overall survival: 2-year and 2.5-year landmark analysis showed encouraging results



Total number of events	63
2-year survival rate (maturity)	79% (50%)
2.5-year survival rate (maturity)	69% (37%)

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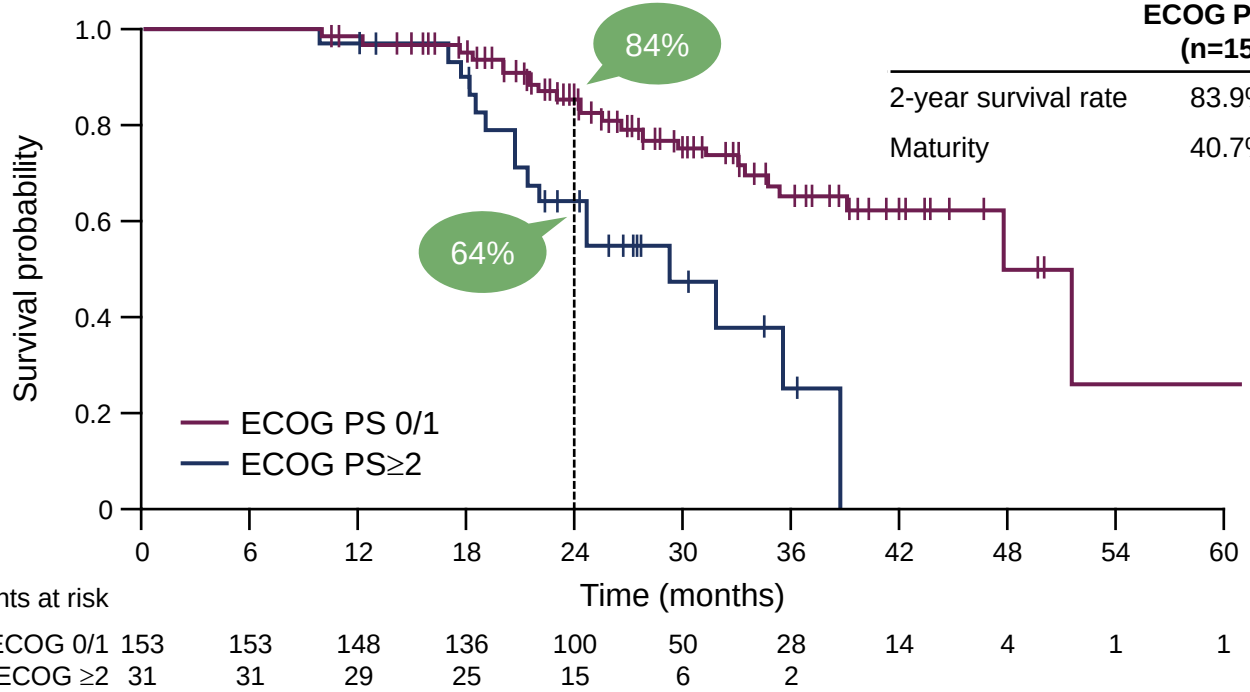
Overall survival: further encouraging results in patients with ECOG PS 0/1



	ECOG PS 0/1 (n=153)	ECOG PS ≥2 (n=31)
2-year survival rate	83.9%	63.5%
Maturity	40.7%	62.5%

Conclusions

- Our results demonstrate the feasibility of sequential afatinib and osimertinib therapy in patients with *EGFR* mutation-positive NSCLC who acquire T790M
- With median time on treatment of 27.6 months in a real-world setting, notably prolonged in Asian patients and those with Del19-positive disease, sequential therapy appears feasible and potentially effective
- While prospective studies are needed to fully determine the optimum treatment strategy, this sequential approach might offer sustained clinical benefit, while avoiding chemotherapy

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