Doelgerichte behandeling

EGFR

dr. A.J. van der Wekken
Longarts-oncoloog

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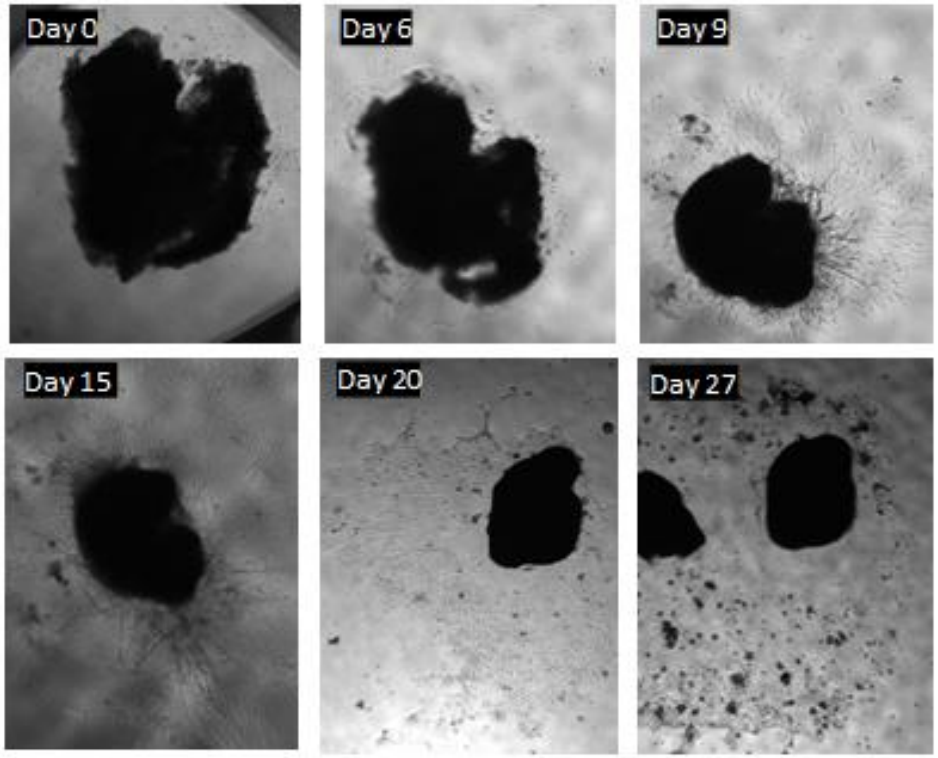
Disclosure

- Advisory board/Lectures:
  - Lilly
  - Boehringer-Ingelheim
  - Pfizer
  - AstraZeneca
  - Roche (diagnostics)
  - Takeda
  - Janssen
- Grant:
  - Boehringer-Ingelheim
  - Pfizer
  - AstraZeneca
  - Roche
  - Takeda

Culture of a primary ROS1-positive tumor sample



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Inleiding

- Welke geneesmiddelen zijn er?
- Wat gebeurt er bij resistentie?
- Welke trials zijn er en waar vind ik deze?

Casus 1 Dhr T 51jr

- Voorgeschiedenis:
- Hypertensie COPD
- 2014 april: bezoek SEH ivm kortademigheid: drainage pleuravocht rechts
- PA: adenocarcinoom van de long

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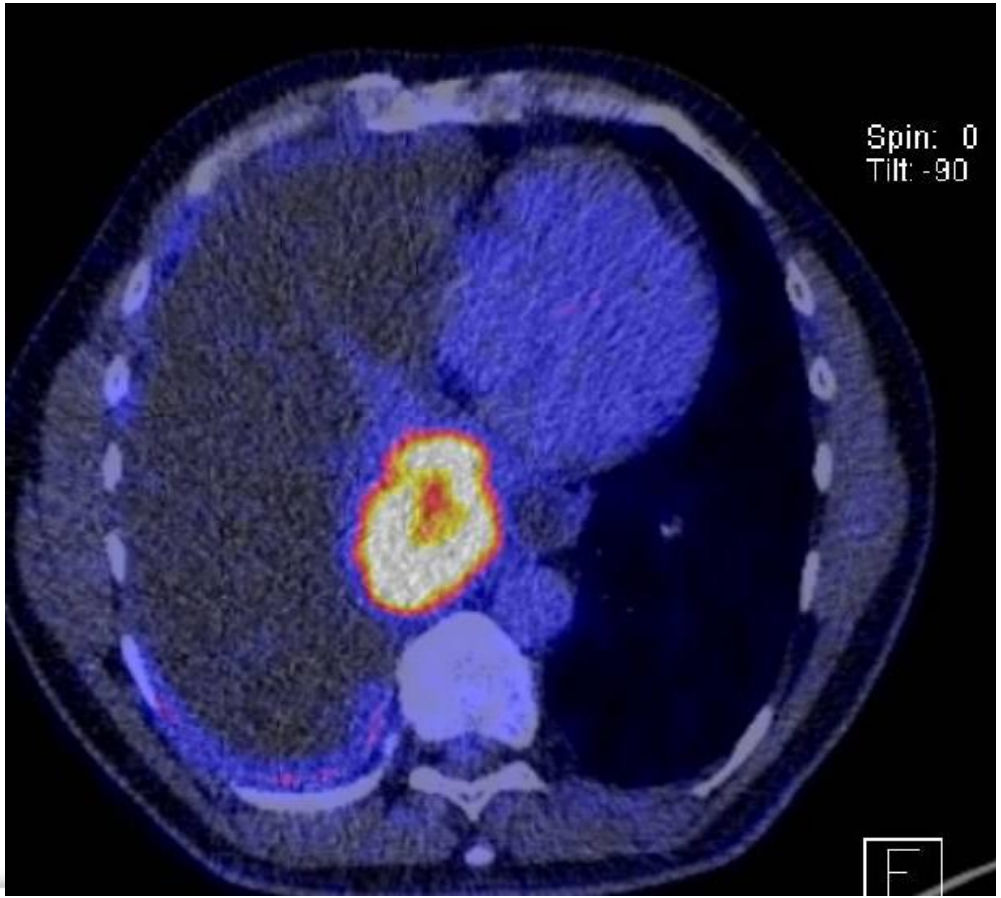

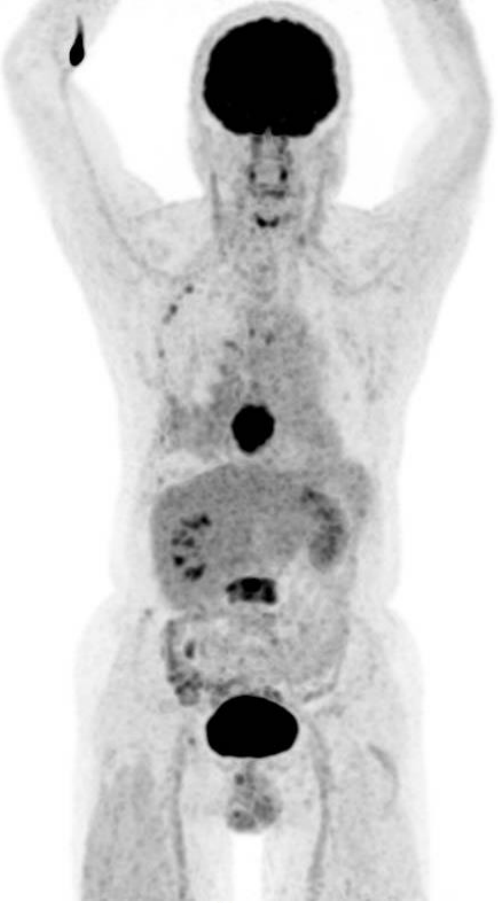

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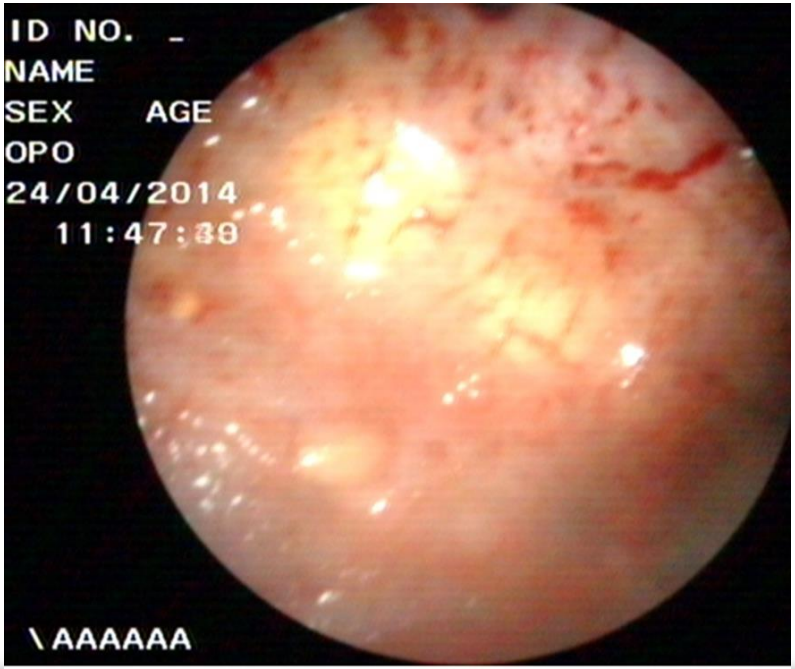
Thoracoscopie



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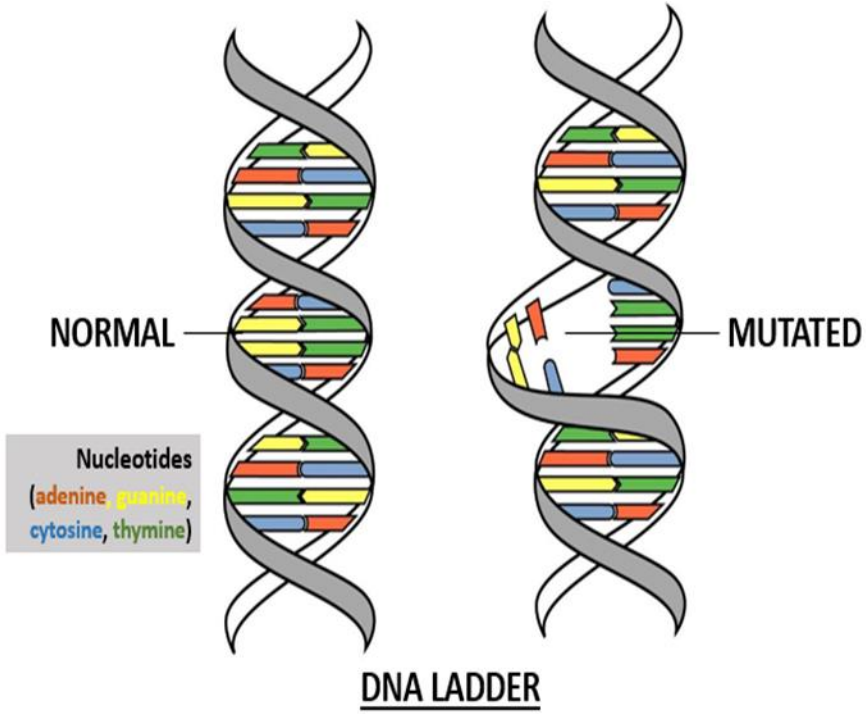
Pathologie verslag

- Biopt dorsale pariëtale pleura rechts: lokalisatie adenocarcinoom
- Mutatie analyse (UMCG): Er is een mutatie aanwezig in exon 19 van het EGFR-gen p.(E746_A750del).

Mutaties

- Verandering in het DNA
- Punt mutatie
- Insertie
- Deletie
- Translocatie
- Duplicatie
- Etc.



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Terug naar de casus

- 1e generatie
  - Erlotinib
  - Gefitinib
- 2e generatie
  - Afatinib
  - Dacomitinib
- 3e generatie
  - Osimertinib

- Combinaties
  - Erlotinib - bevacizumab
  - Erlotinib - ramucirumab

Trial	ORR EGFR TKI	ORR control arm	mPFS EGFR TKI (months)	mPFS control arm (months)	mOS EGFR TKI (months)	mOS control arm (months)
Ipass Gefitinib	71%	47% (chemo)	9.5	6.3	18.8	17.4
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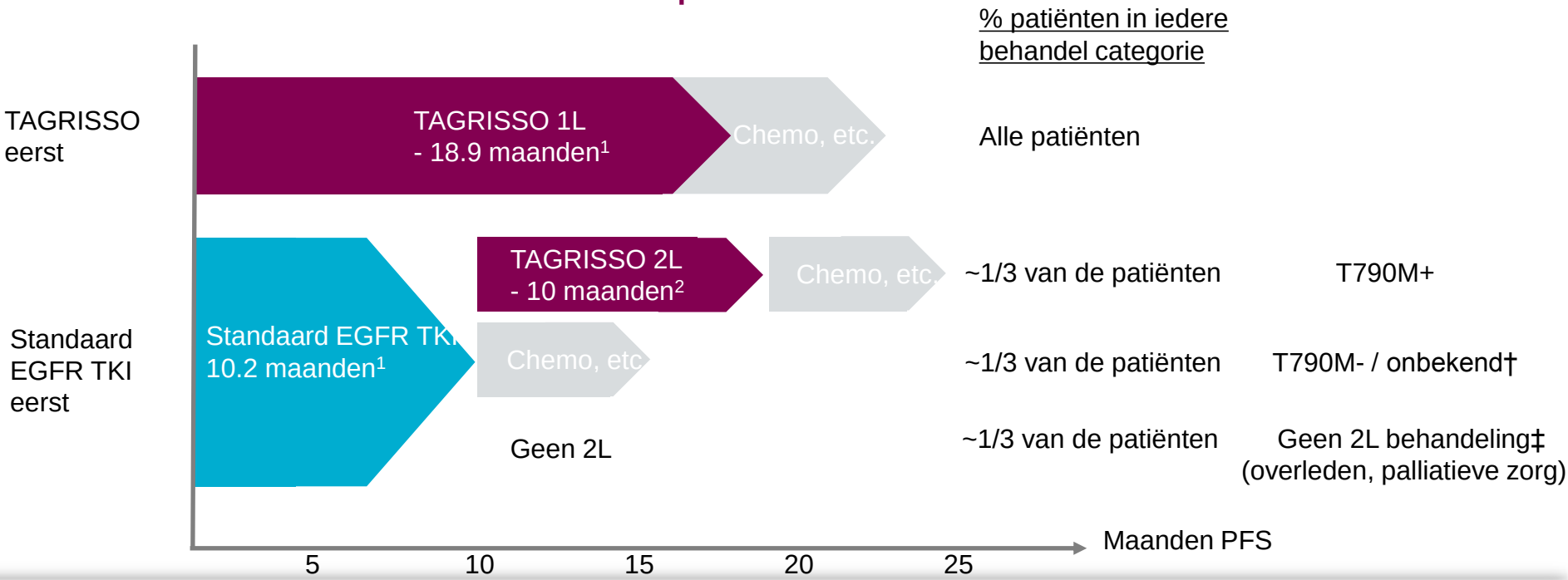
Eerstelijns behandeling met osimertinib geeft PFS voordeel voor alle EGFRm patiënten in FLAURA



1. Ramalingam et al. Presented at ESMO conference: Sept 8-12, 2017; Madrid, Spain. 2. Mok et al. Article and supplementary appendix. N Engl J Med 2017; 376:629-40.
† About 50% EGFRm patients who are tested after progression on 1L EGFR TKI are T790M positive. Also 25% of patients are not eligible for a tissue biopsy upon progression, ~ 20% of re-biopsies yielding sufficient tissue and plasma testing for EGFR T790M mutations only ~ 53% sensitive vs tissue (AURA3).
‡ Across major EGFR TKI studies as in FLAURA ~ 30% of patients on standard EGFR TKIs receive no subsequent cancer therapy – they may die before a recorded progression event or for other reasons (e.g. rapid progression in the brain) receive palliative care only.

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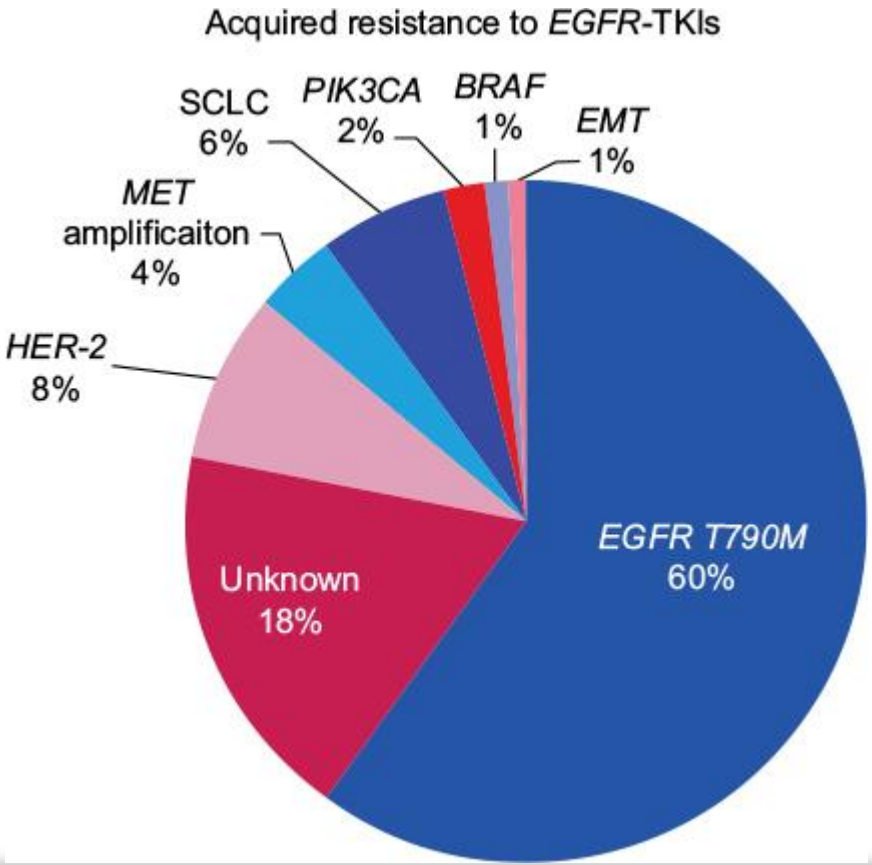

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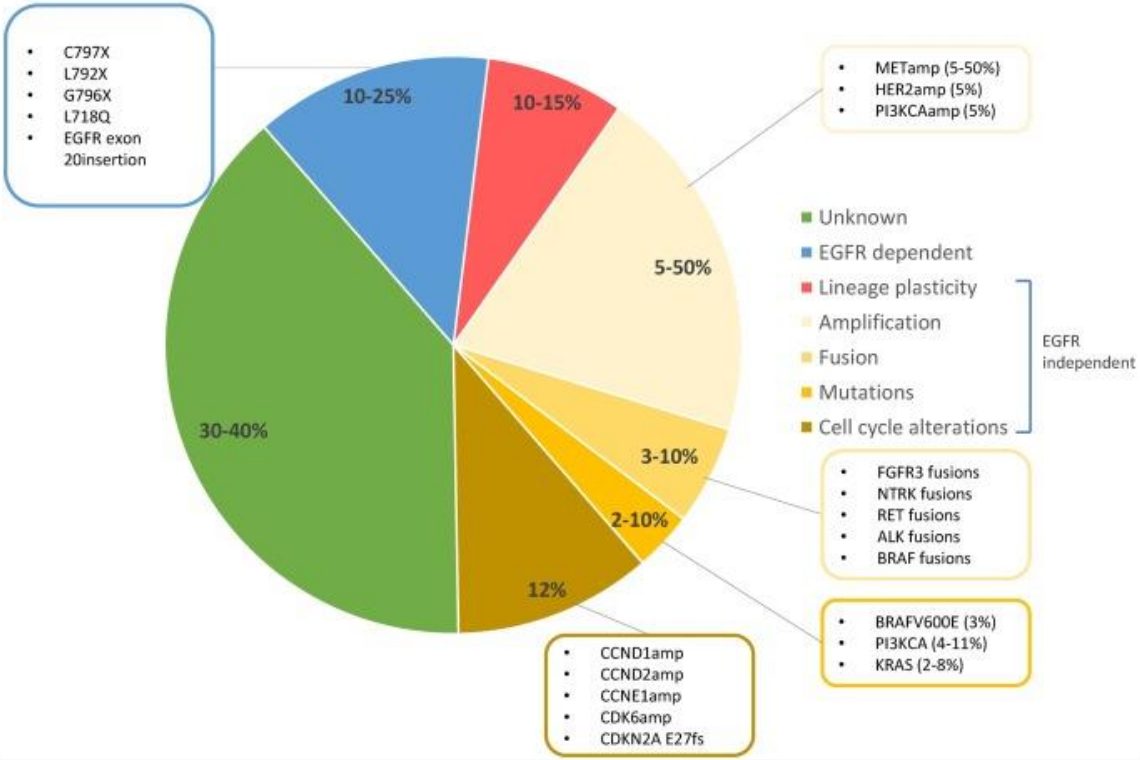
Oxnard et al. JAMA oncol 2018

Resistance Mechanisms To Second-Line Osimertinib



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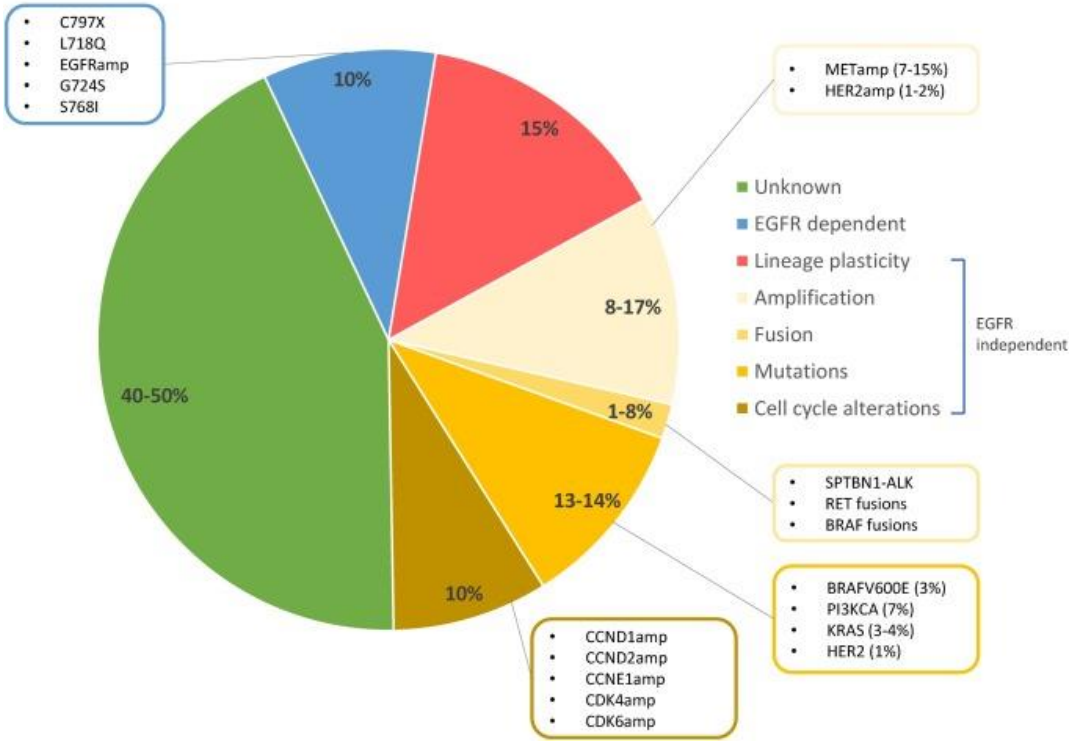
Schmid et al. Lung cancer 2020

Resistance Mechanisms To First-Line Osimertinib



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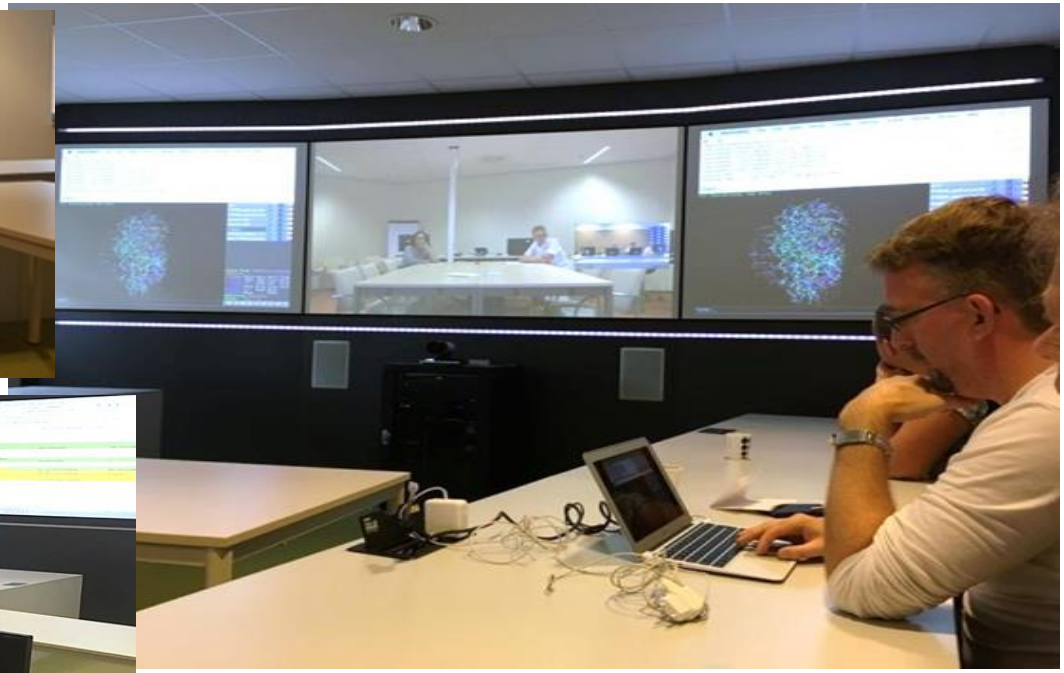
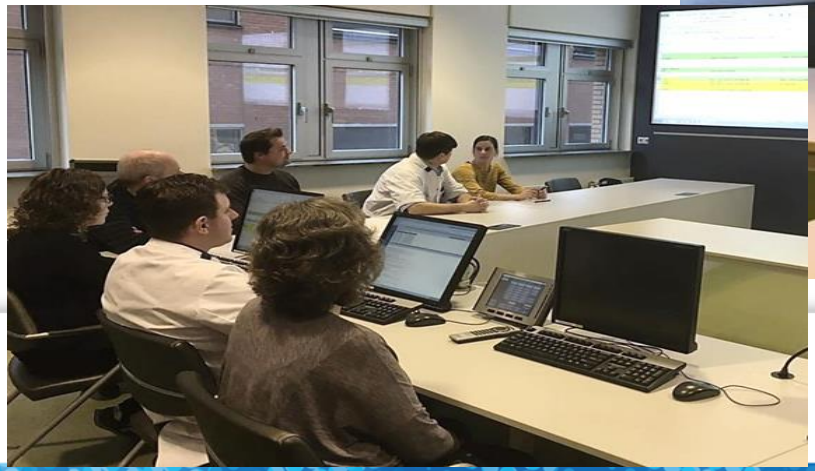
Moleculaire Tumor Board





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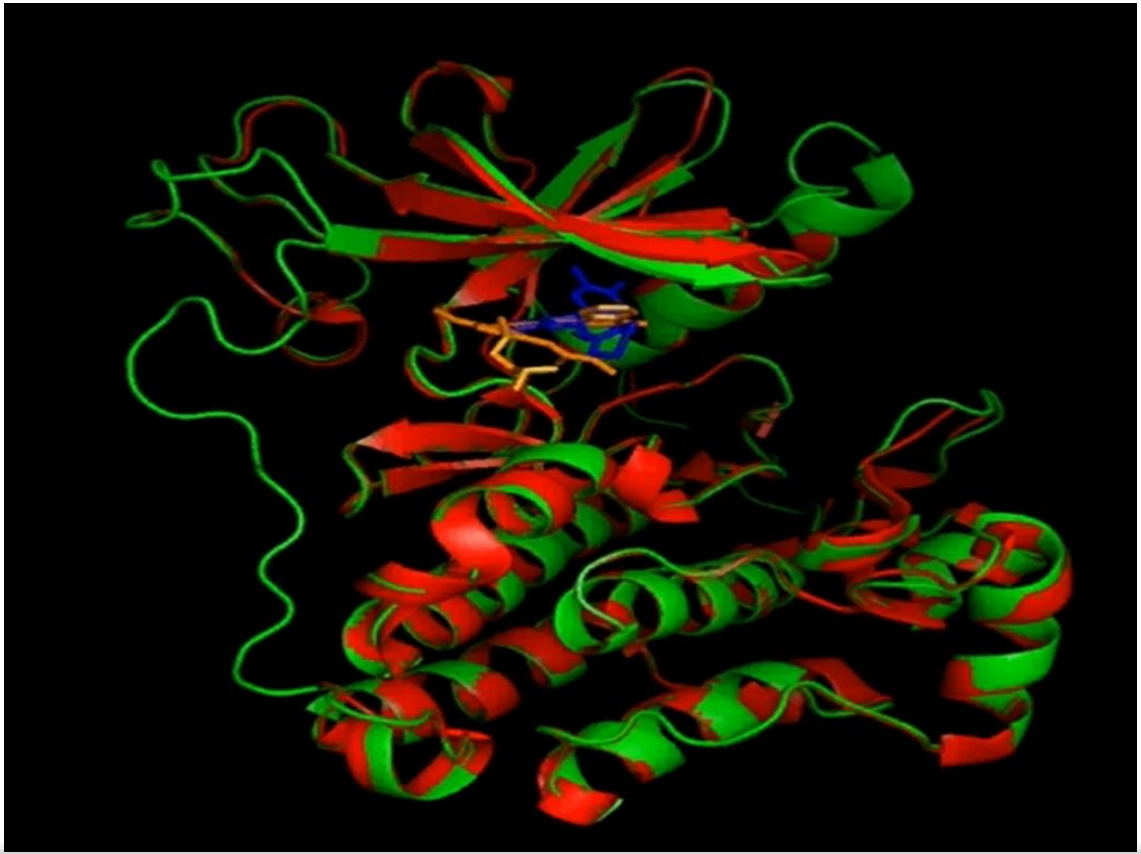

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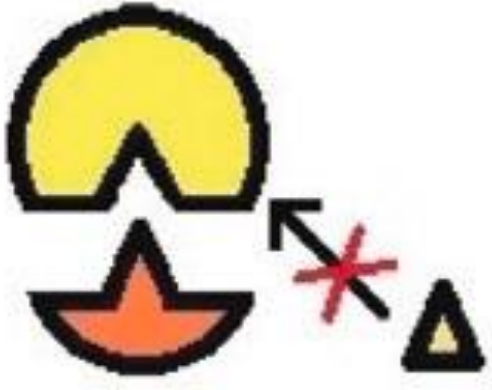
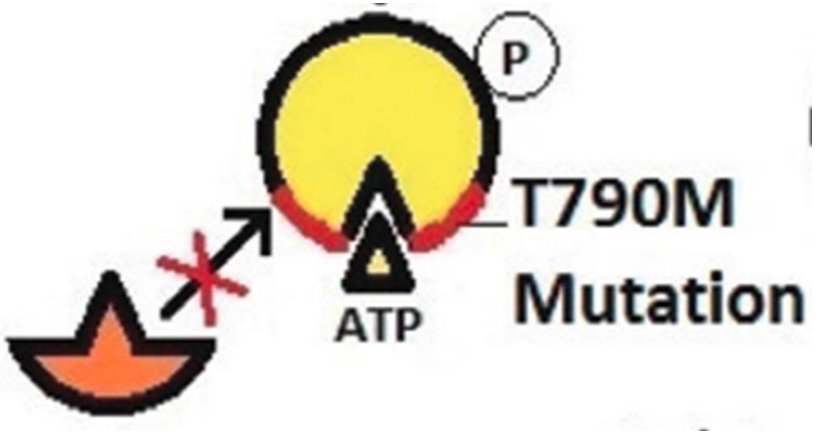
Welke behandeling is mogelijk?



gefitinib of erlotinib



Welke behandeling is mogelijk?

osimertinib

Centra zeldzame mutaties

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Welke studies zijn er?

- 1e lijn therapie
  - Amivantamab vs osimertinib

- Resistentie na EGFR-TKI
  - OSIRIS studie
  - ORCHARD
  - HER2: trastuzumab-emtansine + osimertinib
  - MET: INSIGHT 2 Tepotinib + osimertinib

Welke studies zijn er?

- Exon 20 inserties
  - POSITION 20 – dubbele dosis osimertinib
  - AfaCet – afatinib + cetuximab
  - Poziotinib

Take home message

- Beste therapieën: osimertinib en erlotinib-ramucirumab

- Bij zeldzame mutaties behandeling in centra; daar zijn ook de studies te vinden.

Vragen

- *We dragen allemaal de EGFR factor, maar ergens onderweg gaat er een sneldeelfactor aan. Zou dit met de overgang of hormonen te maken kunnen hebben? of gewoon ouderdom van cellen?*
  - *Er is mogelijk een relatie tussen oestrogeen receptoren en long kanker. De prognose met hoge expressie ER en L858R mutatie lijkt slechter*

- Kunnen bijwerkingen van een TKI ook symptomatisch behandeld worden ipv in zn geheel te stoppen met het middel?

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