

DANSKE KRÆFTFORSKNINGSDAGE 2019

Genomisk profilering og eksperimentel kræftbehandling

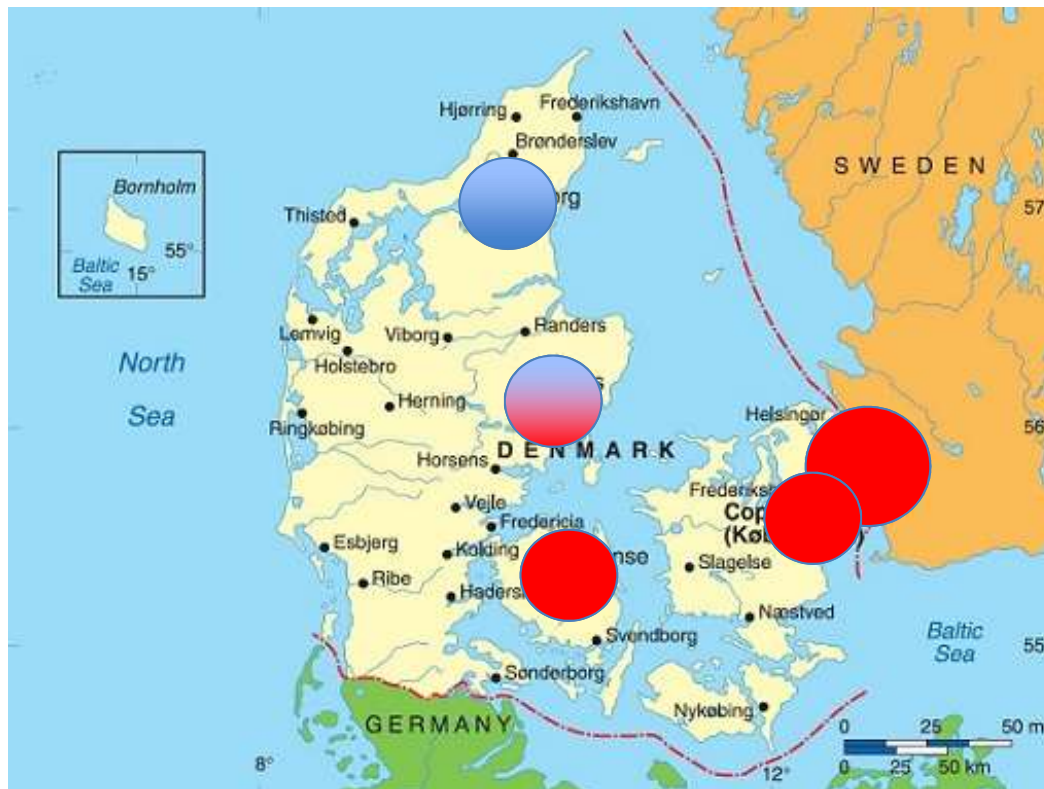
Overlæge PhD, Kristoffer Staal Rohrberg, Fase 1 enheden,
Onkologisk klinik, Rigshospitalet



Professor, overlæge, dr. med. Morten Ladekarl, Onkologisk
afdeling, Aalborg Universitetshospital

ML

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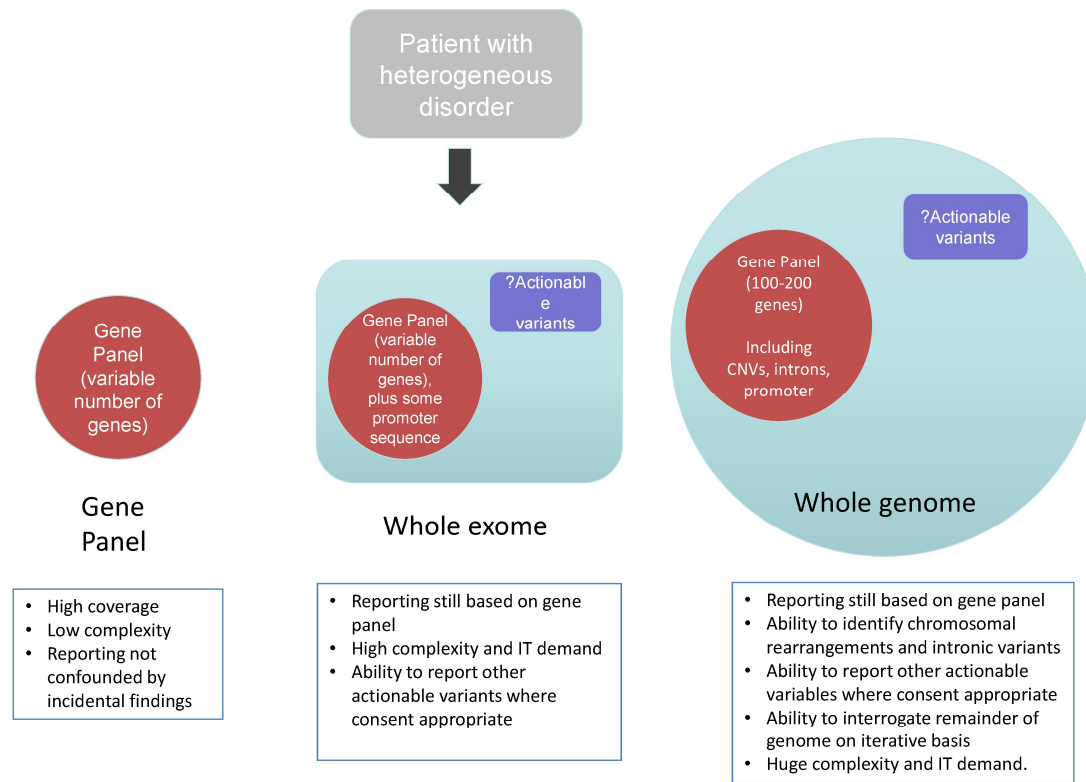
Genomanalyser for kræftpatienter uden yderligere standardbehandling



-  Tilbydes
-  Planlægges

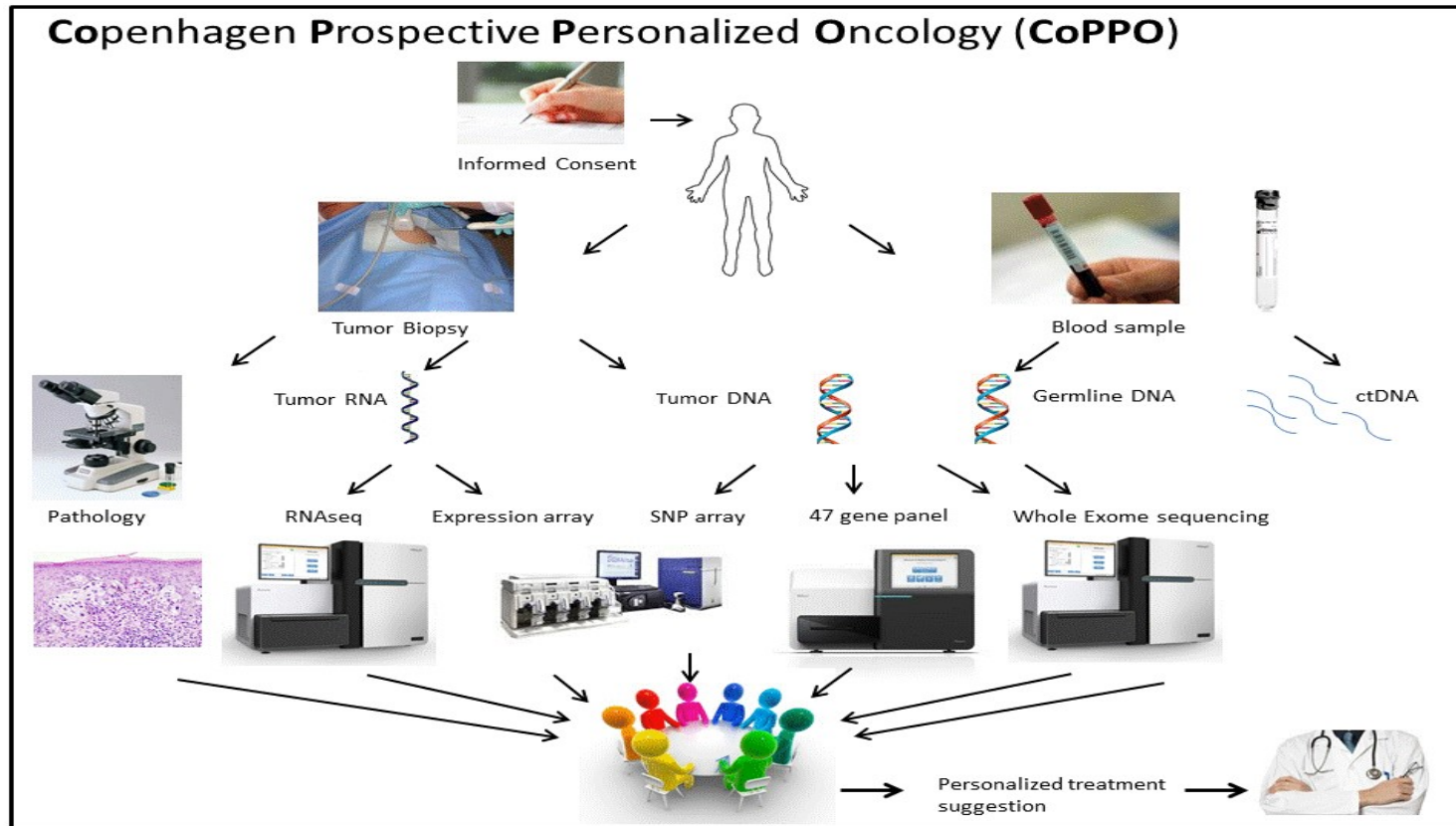
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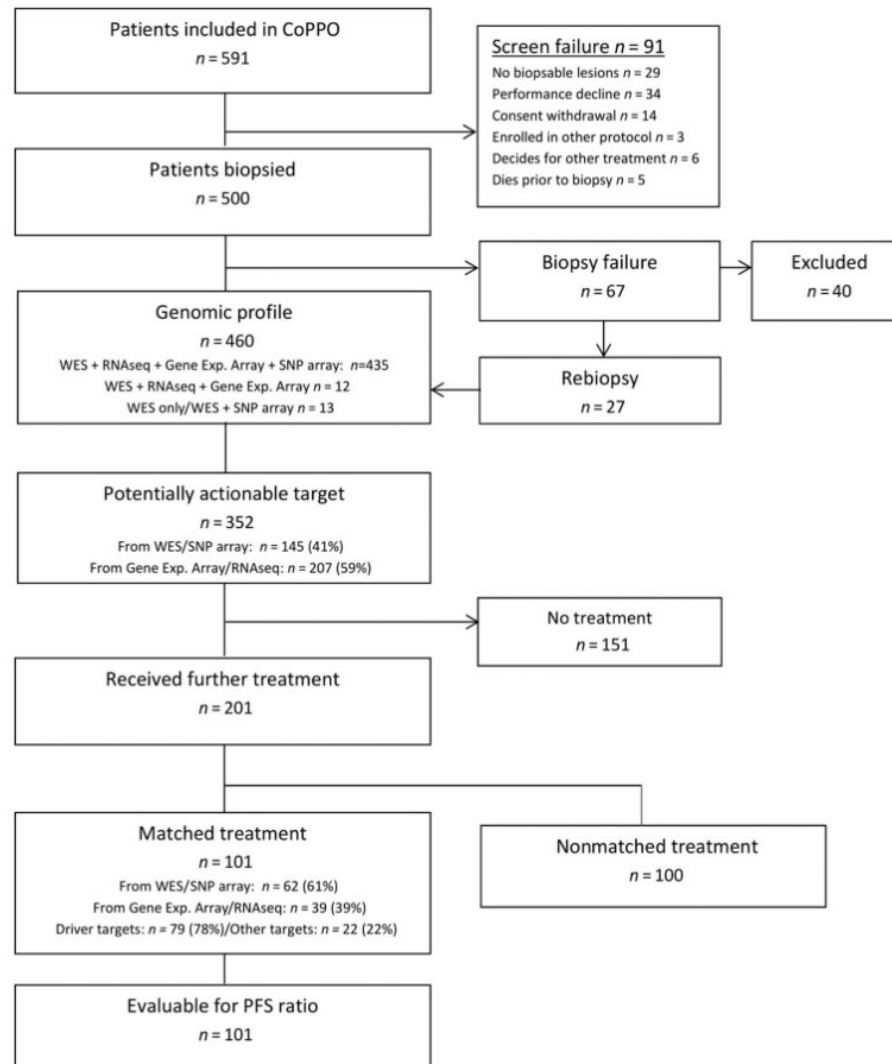
Forskellige muligheder for genanalyser



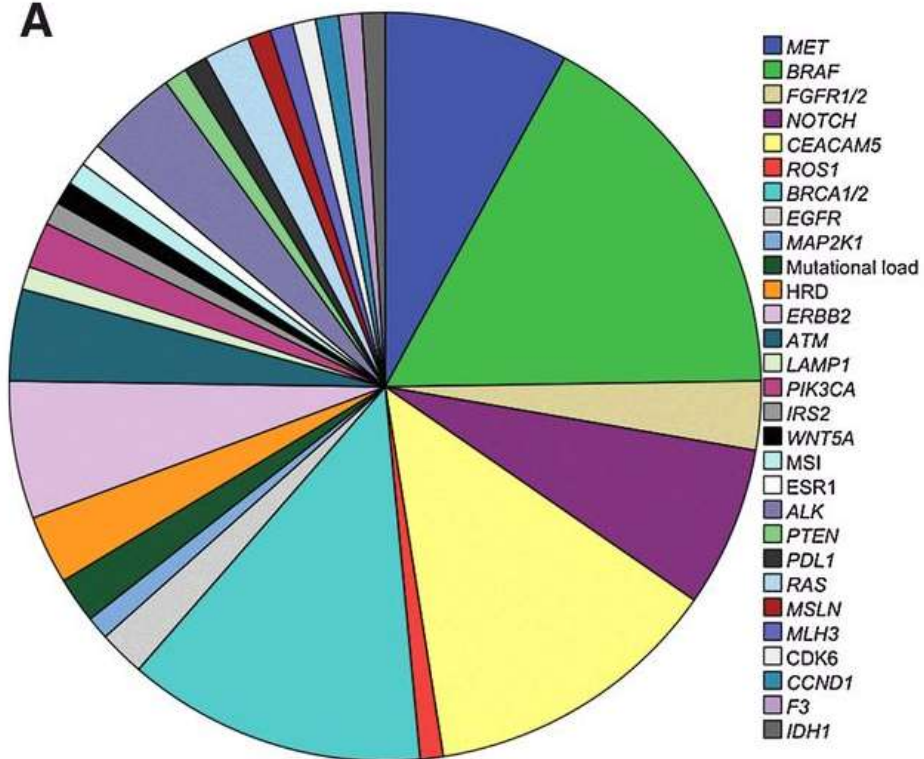
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Genomic profiling at the phase 1 unit RH

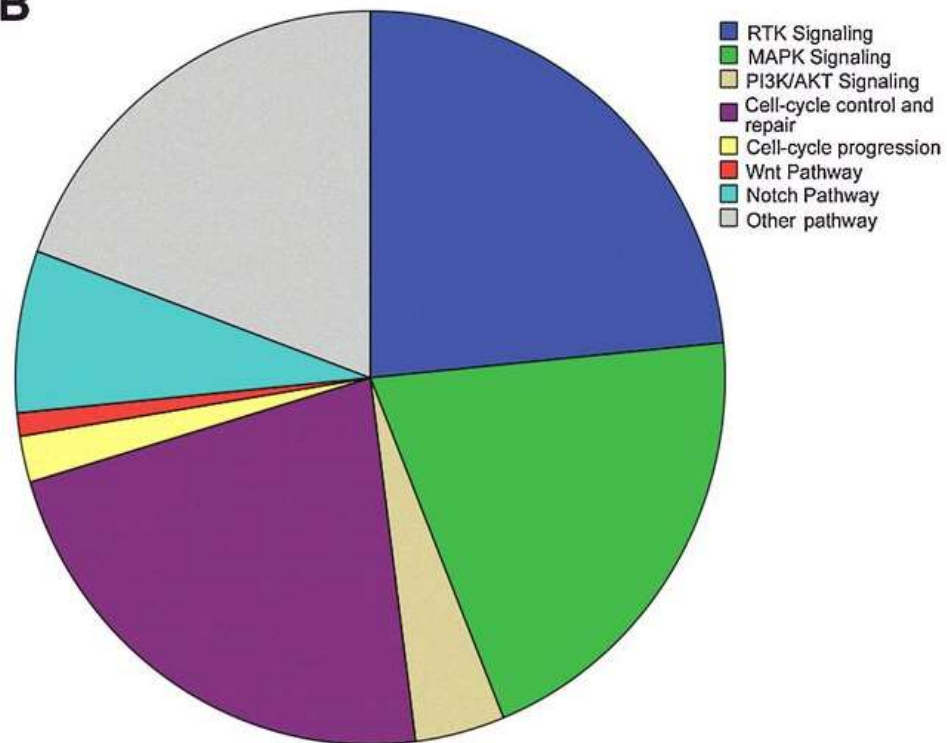


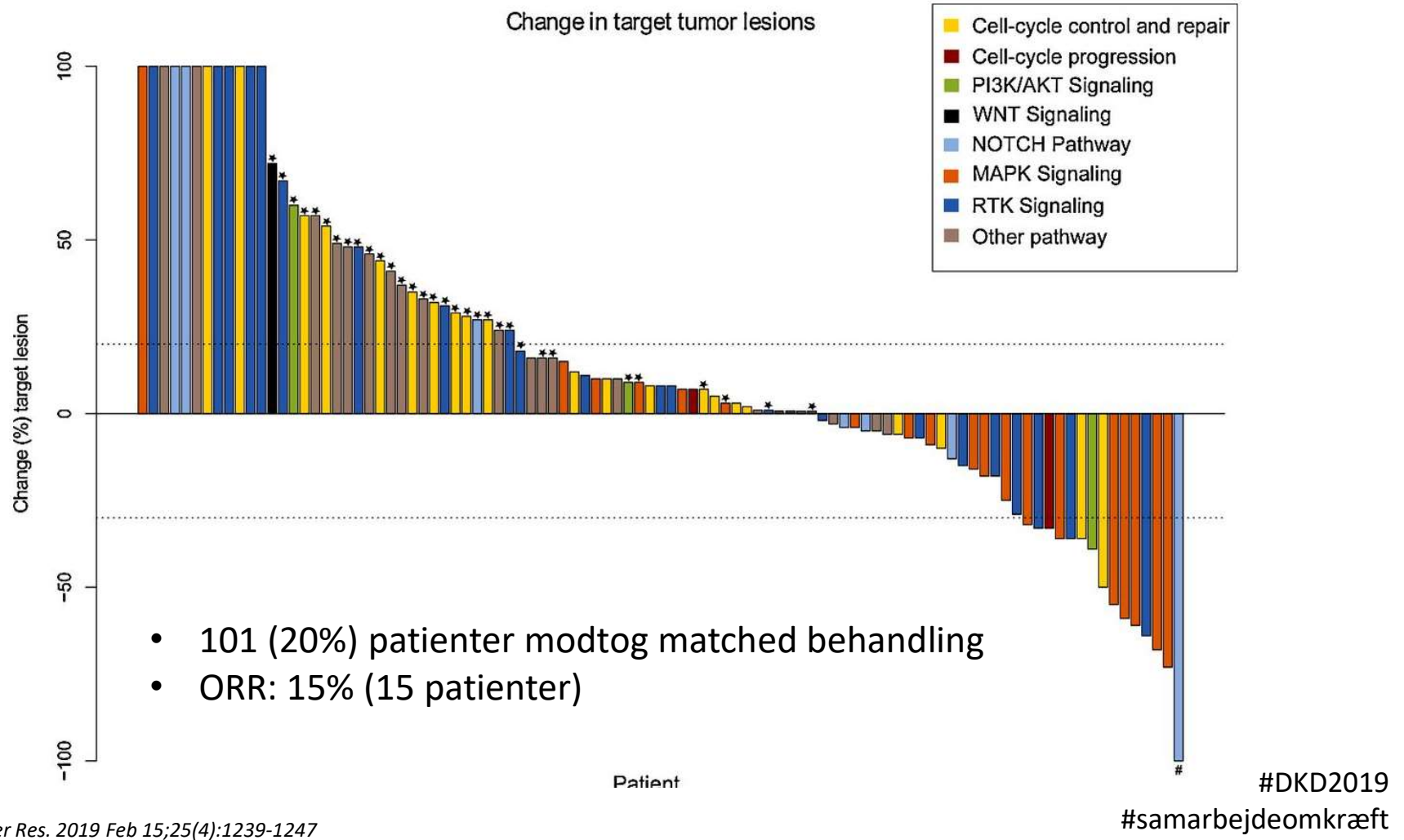


A

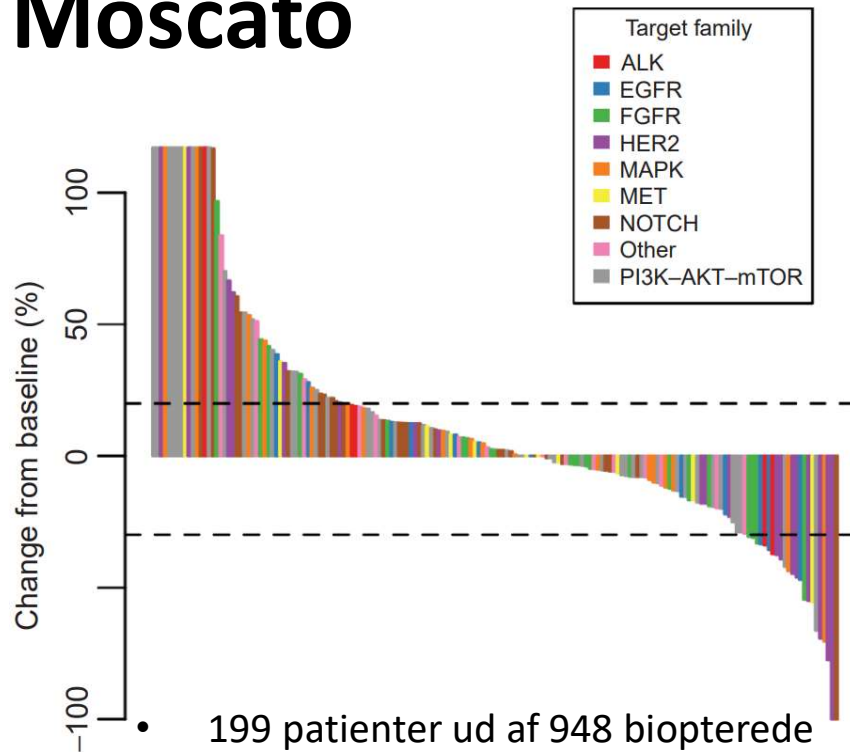


B



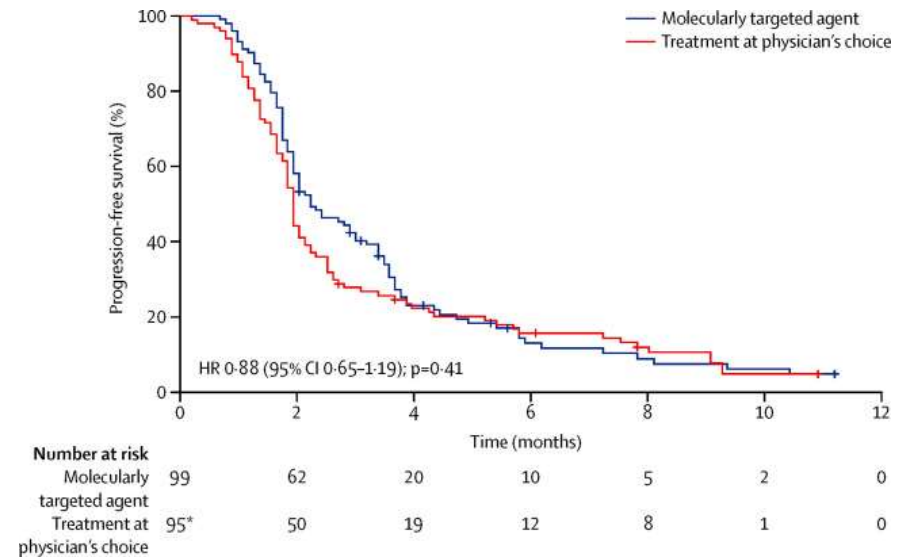


Moscato



- 199 patienter ud af 948 biopterede modtog matchet behandling
- ORR: 11% (22 patienter)

SHIVA

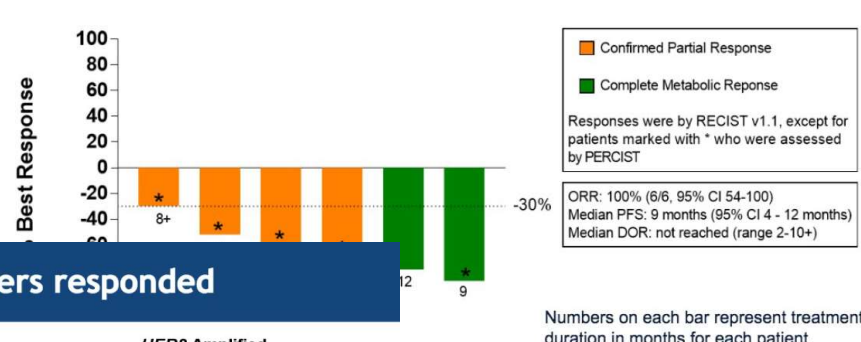
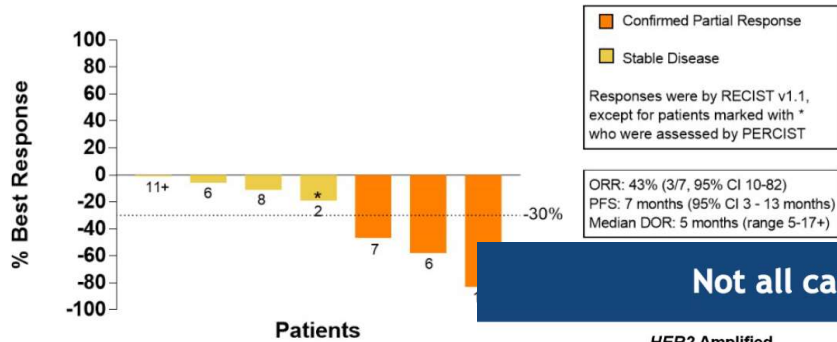


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NCI-MATCH – Trastuzumab-entamcin ved HER-2 amplificeret cancer

HER2 amplified lung cancers

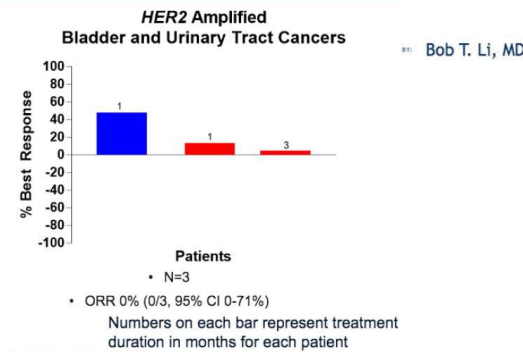
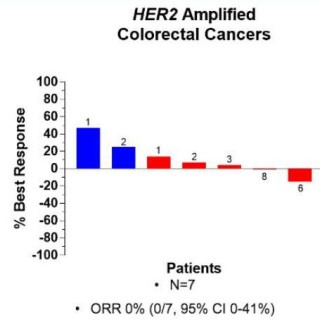
HER2 amplified salivary gland cancers



Not all cancers responded

Numbers on each bar represent treatment duration in months for each patient

PRESENTED AT: 2018 ASCO ANNUAL MEETING #ASCO18
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 PRESENTED BY: Bob T. L



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NATIONAL CANCER INSTITUTE NCI-MATCH CLINICAL TRIAL

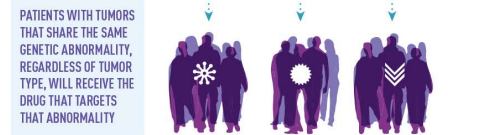
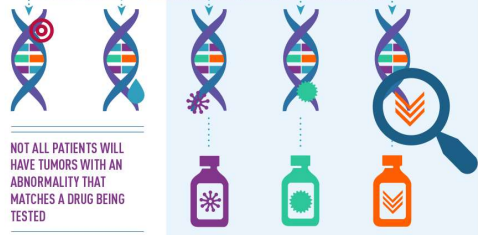
THIS PRECISION MEDICINE TRIAL EXPLORES TREATING PATIENTS BASED ON THE MOLECULAR PROFILES OF THEIR TUMORS

NCI-MATCH* IS FOR ADULTS WITH:

- solid tumors (including rare tumors) and lymphomas
- tumors that no longer respond to standard treatment



IF A PATIENT'S TUMOR HAS A GENETIC ABNORMALITY THAT MATCHES ONE TARGETED BY A DRUG USED IN THE TRIAL, THE PATIENT WILL BE ELIGIBLE TO JOIN THE TREATMENT PORTION OF NCI-MATCH

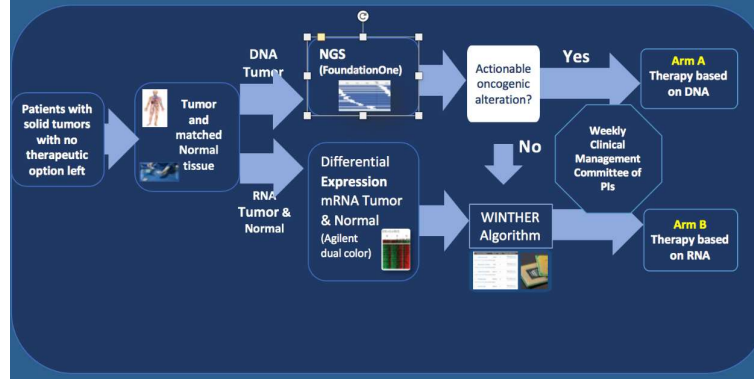


*NCI-Molecular Analysis for Therapy Choice

www.cancer.gov/nci-match
To learn more, call 1-800-4-CANCER

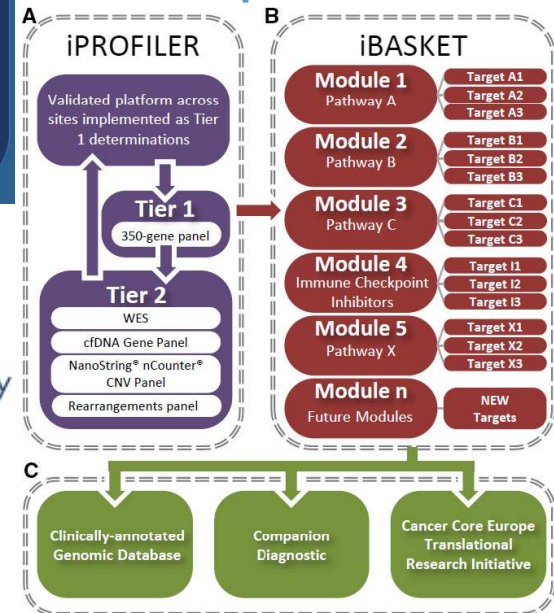


WINTHER Trial - Workflow



ASCO TAPUR™

Targeted Agent and Profiling Utilization Registry Study



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National MDT for personlig medicin

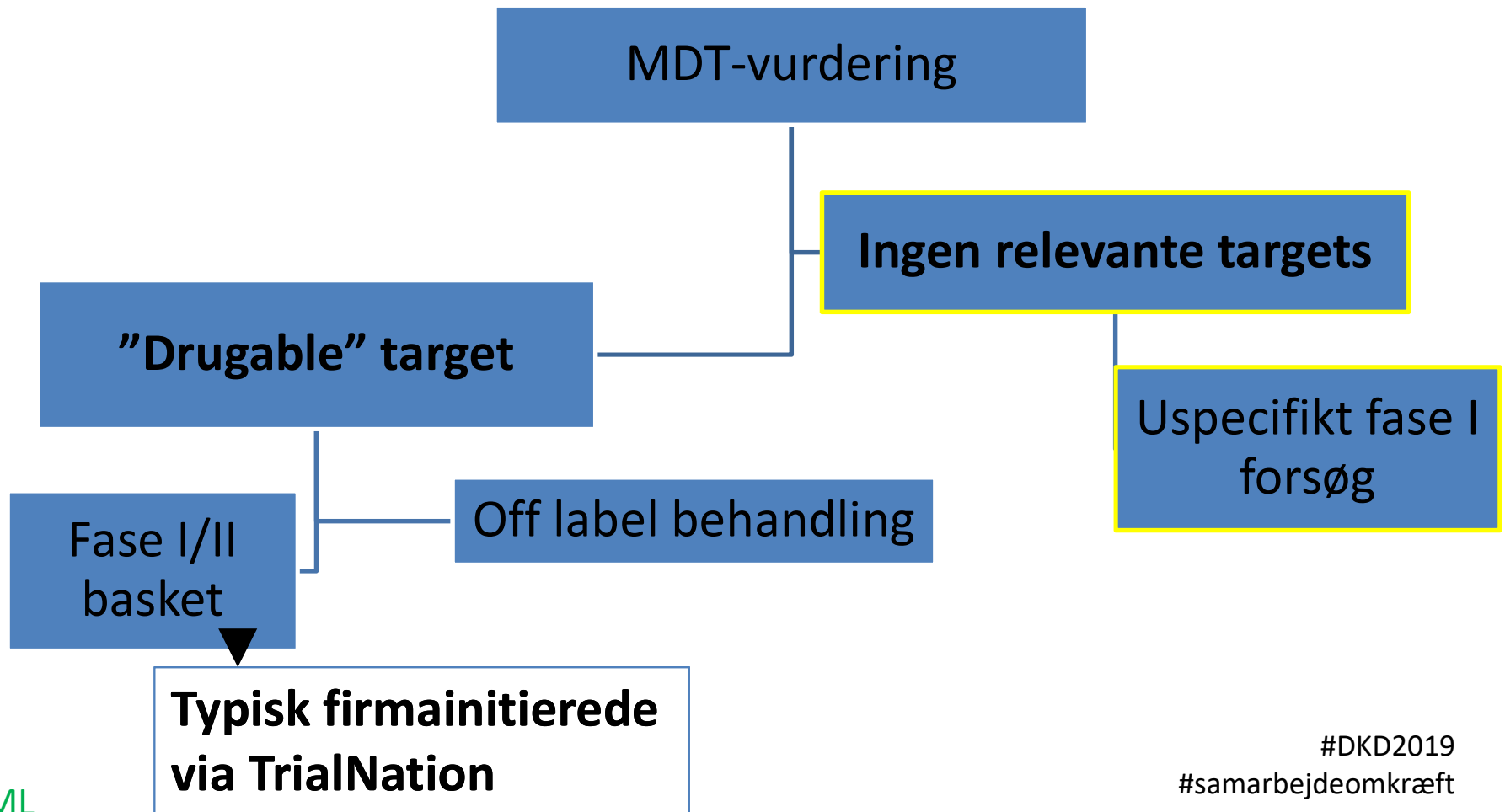
Onkologi
Hæmatologi
Pædiatri

Molekylærbiologi
Farmakologi
Bioinformatik

Rigshospitalet
Århus Universitetshospital
Aalborg Universitetshospital
Odense Universitetshospital
Herlev Sygehus

Klinisk
Genetik

Patologi



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Eksempel: FUZE basket protokol

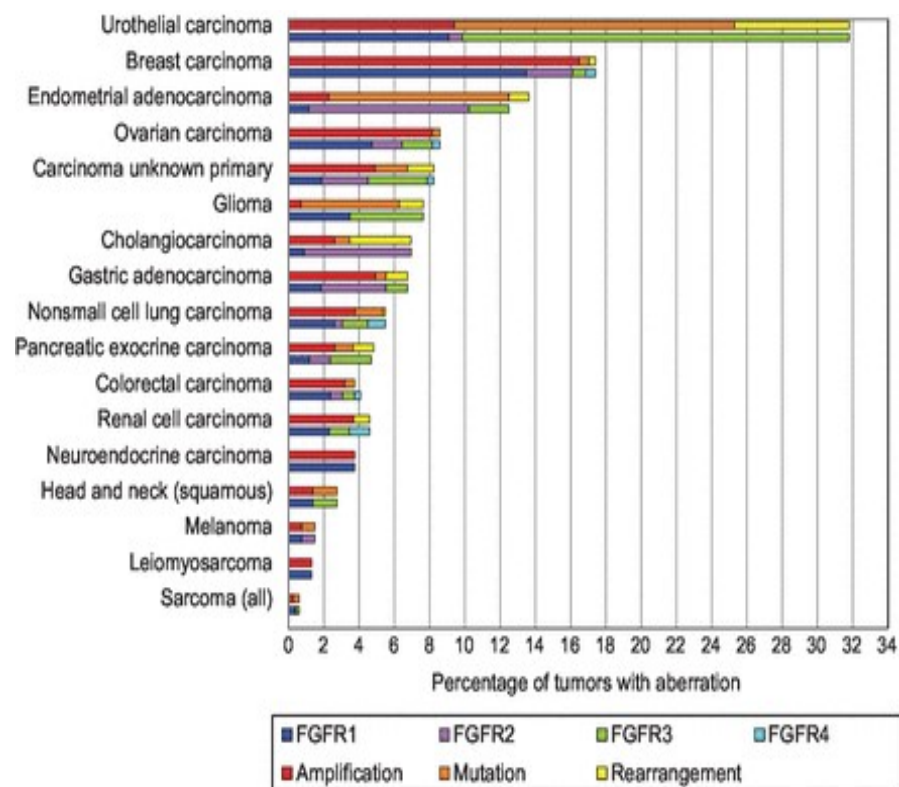
Sponsor: Debiopharm

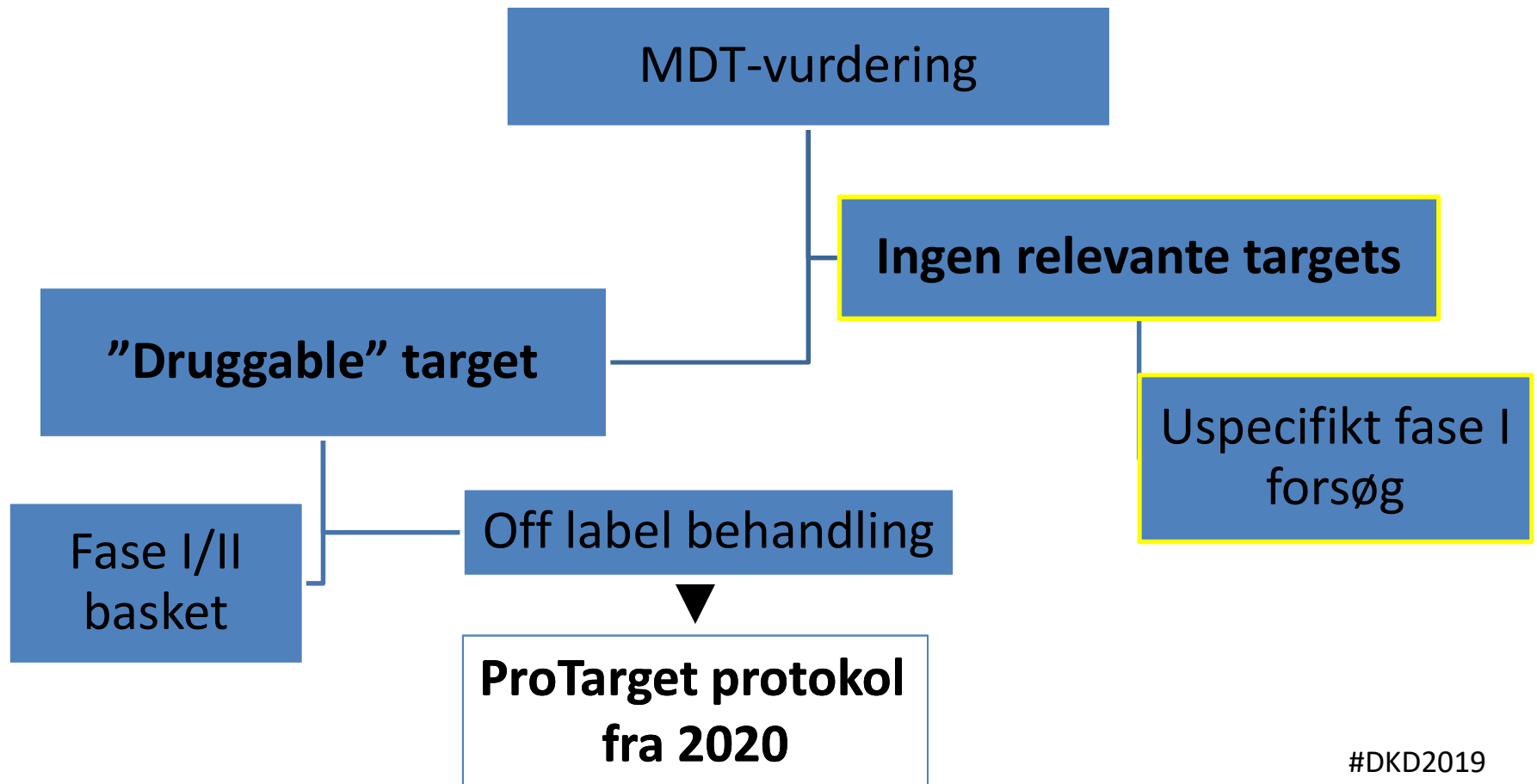
Drug: Oral pan-FGFR inhibitor

Inklusion: FGFR1-3 fusionsgen,
PS 0-1, målbar sygdom

Fase I-forsøg med 57 pt. viste PR
hos 6 og SD hos 16 pt.

Clin Cancer Res; 22(1) January 1, 2016





ProTarget: A Danish Nationwide Clinical Trial on Targeted Cancer Treatment based on Genomic Profiling

PI: Ulrik Lassen, RH. **Co-PI:** Herlev, Odense, Århus, Aalborg, Vejle.

Primary Objectives:

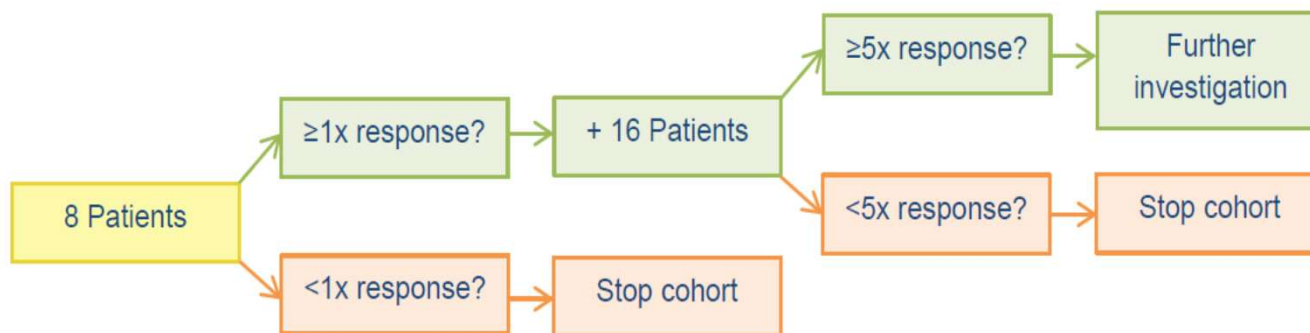
To evaluate the anti-tumor activity and toxicity of commercially available, targeted anti-cancer drugs used for treatment of patients with an advanced solid tumor, multiple myeloma or B cell non-Hodgkin lymphoma that harbours a genomic- or protein expression variant known to be a drug target or to predict sensitivity to a drug.

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ProTarget:

”One diagnosis – one target – one drug*”



Samkøres med amerikanske “Tapur” og hollandske “DRUP”

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* EMA-godkendte stoffer fra samarbejdende medicinalfirmaer

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TRK Fusions Found in Diverse Cancer Histologies

TRK FUSION FREQUENCY

<5%

CNS

- ✓ Astrocytoma
- ✓ Brain low-grade glioma
- ✓ Glioblastoma

GI

- ✓ Colorectal cancer
- ✓ Cholangiocarcinoma
- ✓ GIST
- ✓ Pancreatic cancer

Head and neck

- ✓ Squamous cell carcinoma

Lung

- ✓ Adenocarcinoma
- ✓ Large cell neuroendocrine

Other

- ✓ Acute myeloid leukemia
- ✓ Breast invasive carcinoma
- ✓ Melanoma
- ✓ Sarcoma

5–25%

- ✓ Congenital mesoblastic nephroma
- ✓ Papillary thyroid cancer
- ✓ Pontine glioma
- ✓ Spitz tumors

>75%

- ✓ Mammary analogue secretory carcinoma (MASC) of the salivary glands
- ✓ Secretory breast carcinoma
- ✓ Infantile fibrosarcoma

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Case: Targeting HER-2 in rectum cancer

- 70 year-old woman diagnosed 2013 with rectal adenocarcinoma with syncroneous lung and liver metastases
- RAS wt, BRAF gene status normal, pMMR
- Exposed for 5FU, irinotecan, oxaliplatin, bevacizumab, panitumumab and lonsurf

Morten Ladekarl and Britt E. Lauersen



NORTH DENMARK REGION



Genomic analysis (WES)

- MSS, mutational rate moderately high
- Mutations in TP53 and CTNNB1
- Amplification of ERBB2, EGFR, CCND2, TERT, RICTOR, MEW.1D, CDK12, NF1, SMARCE1
- No gene fusions

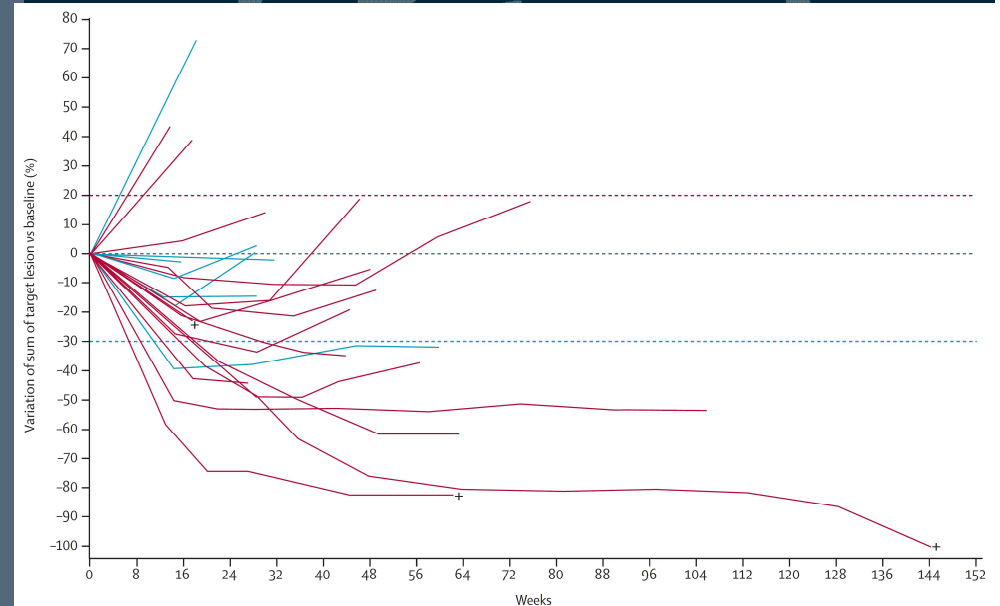


MDT

- ERBB2 amplification and/or HER2 overexpression in 5%
- Phase II-studies of HER2-targeted treatment with trastuzumab and lapatinib
- Confirmatory IHC: HER2-receptor status 3+

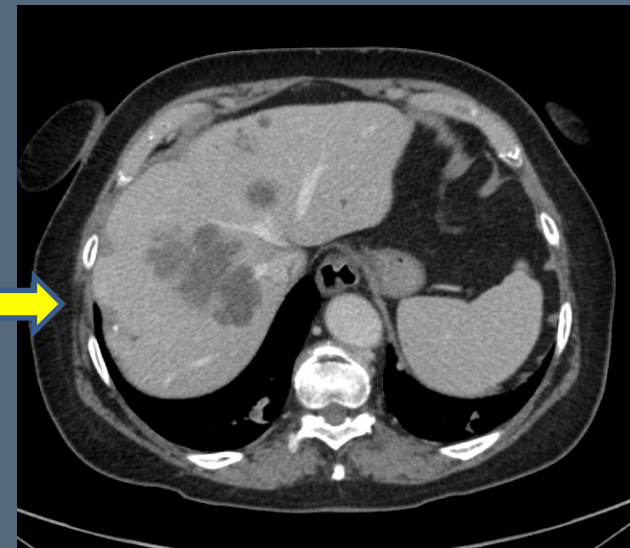
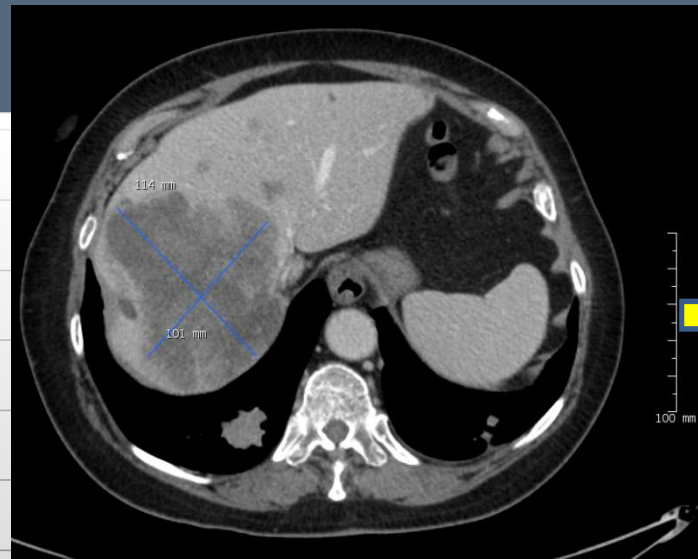
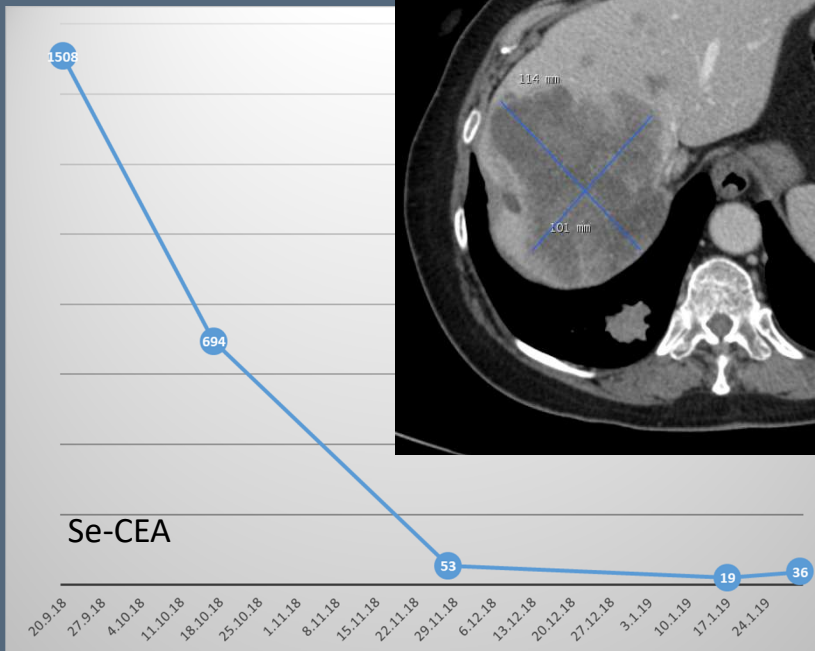
Dual-targeted therapy with trastuzumab and lapatinib in treatment-refractory, KRAS codon 12/13 wild-type, HER2-positive metastatic colorectal cancer (HERACLES): a proof-of-concept, multicentre, open-label, phase 2 trial

Andrea Sartore-Bianchi, Livio Trusolino*, Cosimo Martino, Katia Bencardino, Sara Lonardi, Francesca Bergamo, Vittorina Zagonel, Francesco Leone, Ilaria Depetris, Erika Martinelli, Teresa Troiani, Fortunato Ciardiello, Patrizia Racca, Andrea Bertotti, Giulia Siravegna, Valter Torri, Alessio Amatu, Silvia Ghezzi, Giovanna Marrapese, Laura Palmeri, Emanuele Valtorta, Andrea Cassingena, Calogero Lauricella, Angelo Vanzulli, Daniele Regge, Silvio Veronese, Paolo M Comoglio, Alberto Bardelli*, Silvia Marsoni*, Salvatore Siena*





Partial Response after 8 weeks on treatment



33% diff. in sum of total diameters
Symptomatic response after 2 weeks