Bridging the gap between Regulatory approval & Reimbursement for Precision Medicines: a case study from the Netherlands

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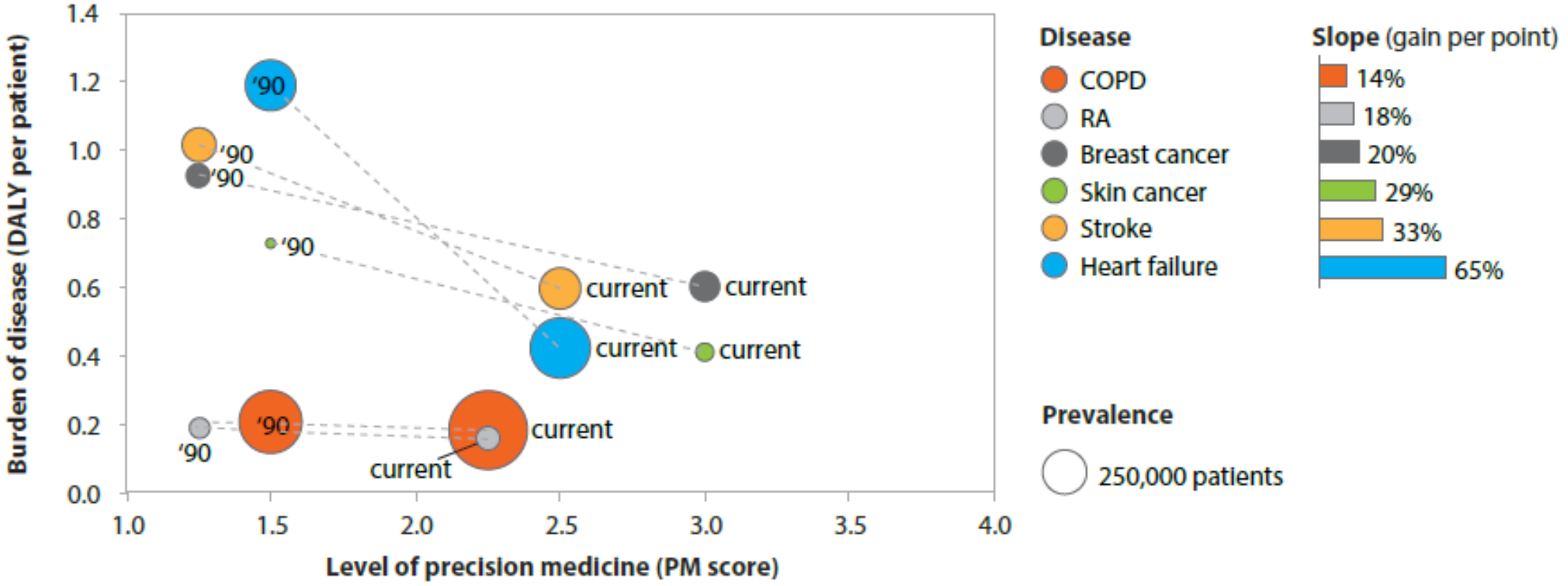
Disclosures

Janneke Boersma is an employee of Roche Nederland B.V.
The views expressed in this presentation and panel discussion are her personal opinions

Care has become more personalised in various disease areas in the Netherlands, since 1990

Relationship between level of precision medicine and burden of disease in the Netherlands

[level of precision medicine in PM score, burden of disease in DALY/patient, 1990 - 2017]



N=1, PHC Catalyst Alliance, Gupta

Imagine the potential of PHC in the Netherlands…
if all existing cutting edge technology and advancements are implemented

2 to 4 extra weeks
in good health each year

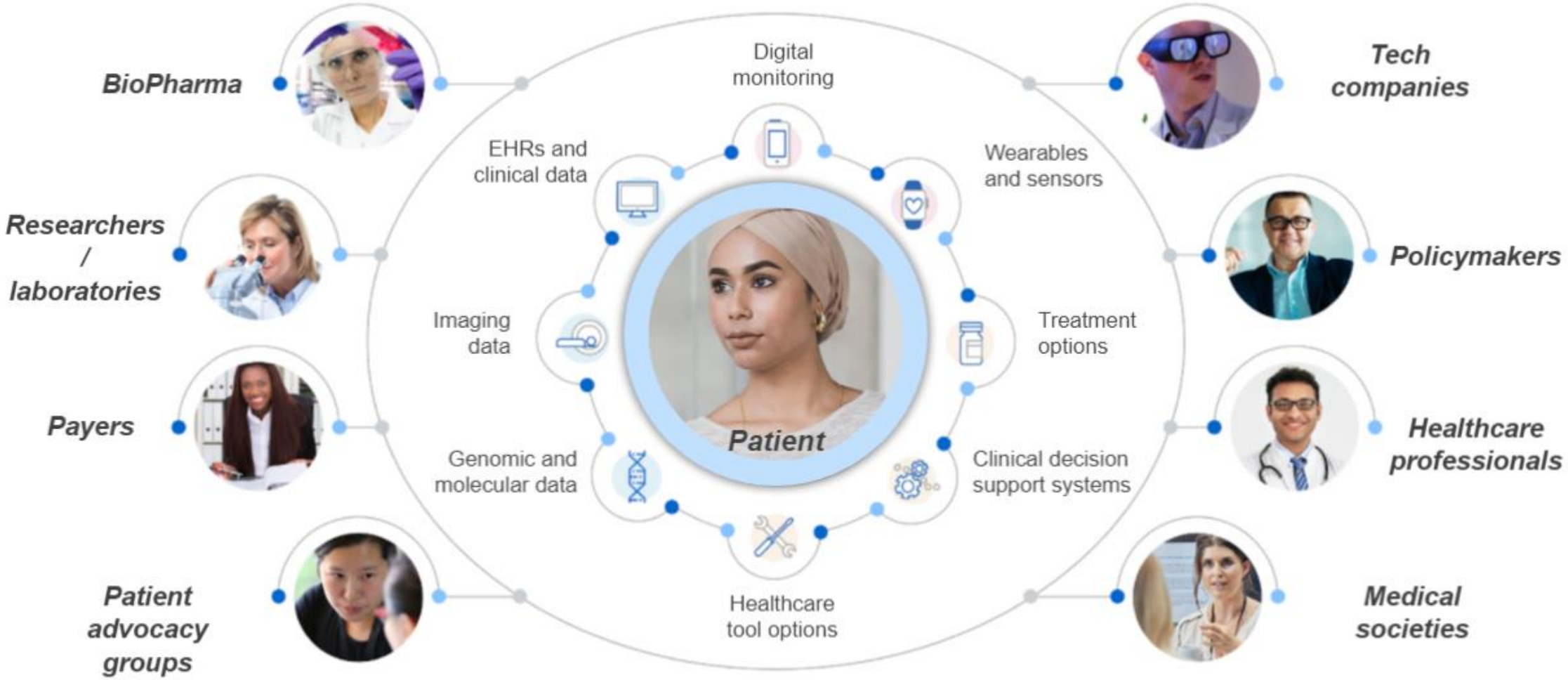
3 to 7 extra years
in good health
over a lifetime

≈

An enormous potential.
Imagine there was **no more disease south of the Rhine**

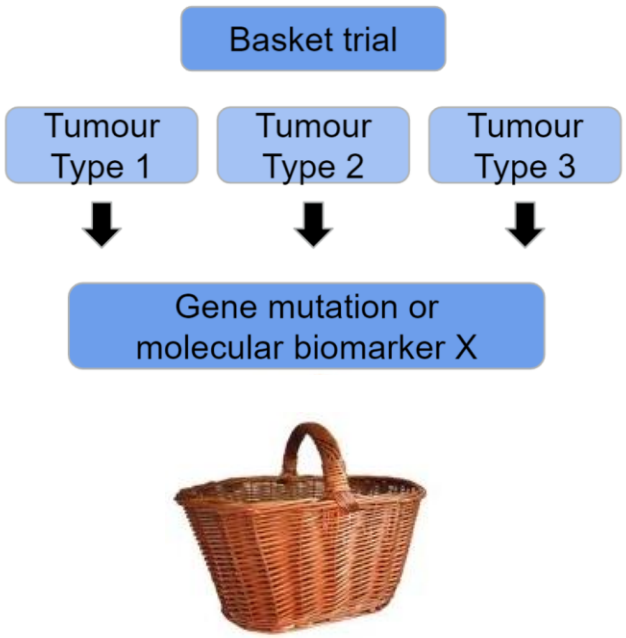
N=1, PHC Catalyst Alliance, Gupta

Realisation of the promise of PHC takes an integrated approach and many paradigm shifts



EHR, electronic health record

Cancer a disease of the genome: from tumour type to tumour biology



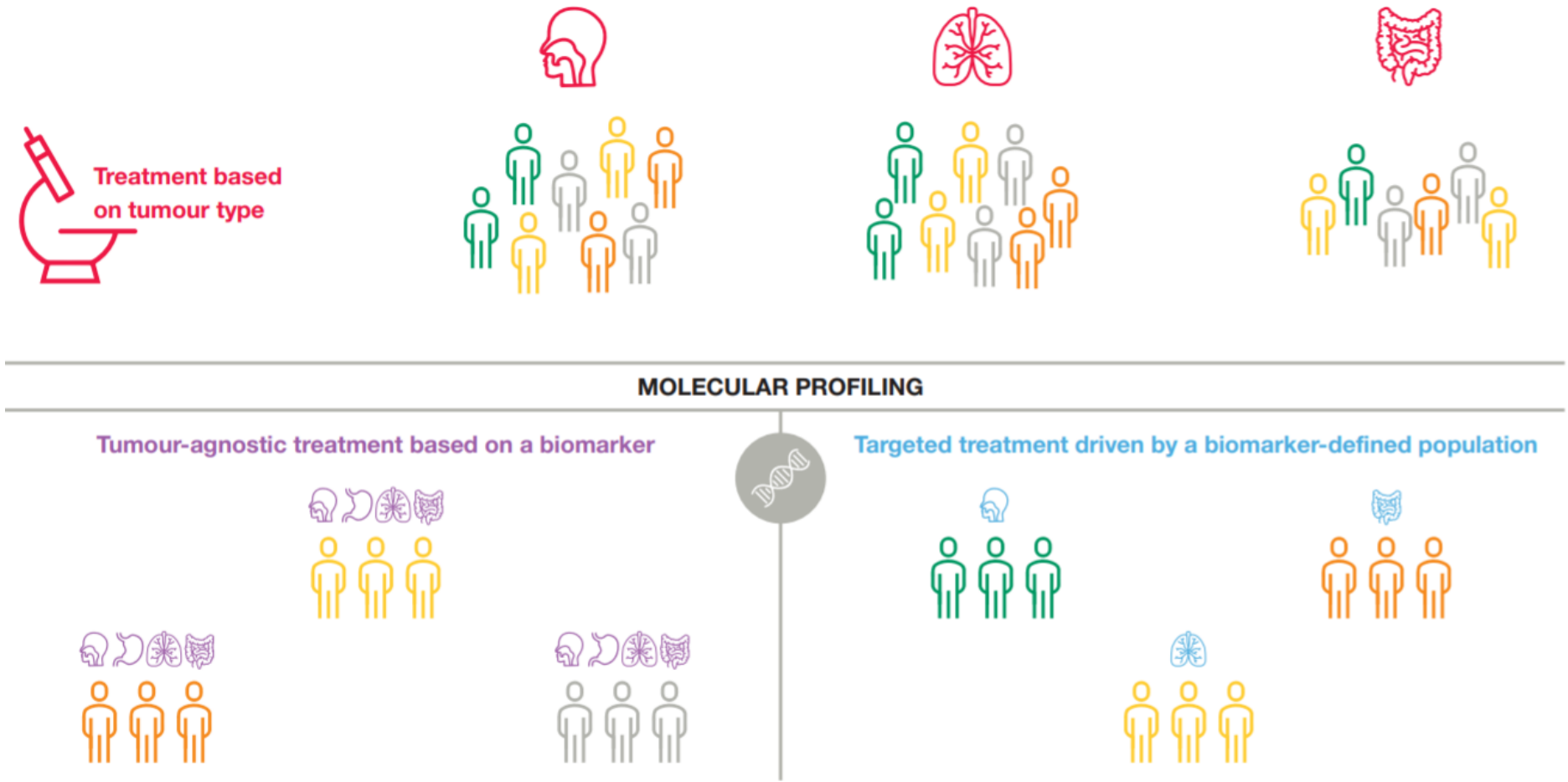
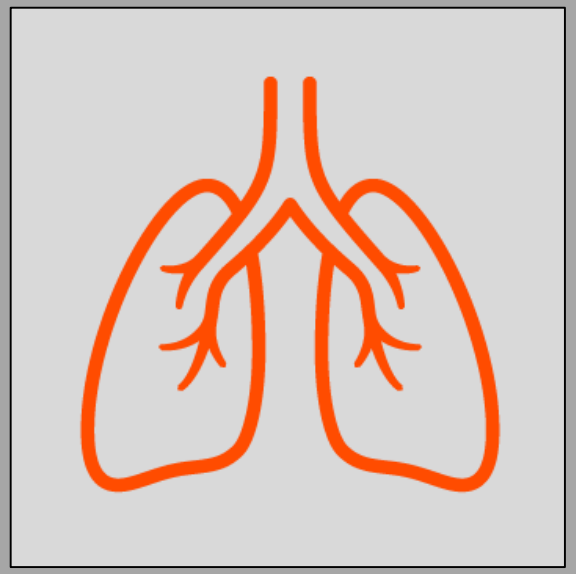


Figure 2. Personalising cancer treatment informed by in-depth characterisation of tumour genomic alterations.

Thomas et al. Aiming for higher ambition: the Roche approach to cracking the code of cancer, Nature Research



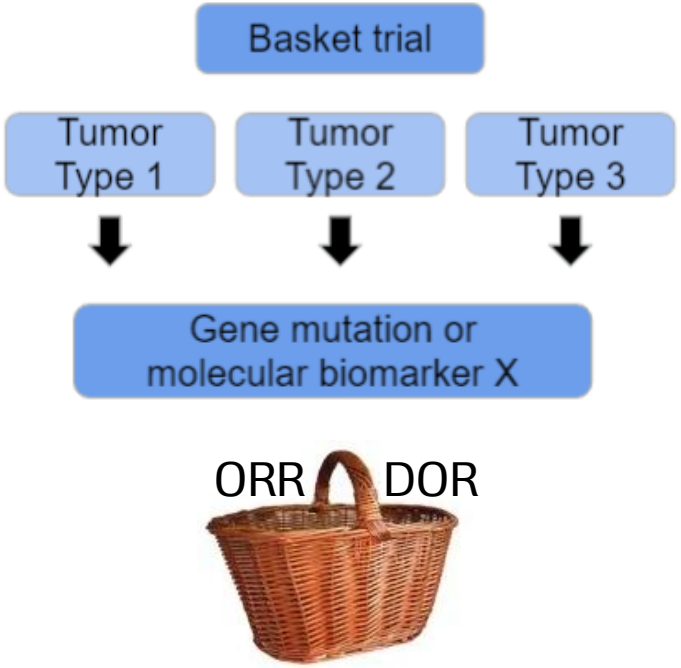
ALK+
5% NSCLC

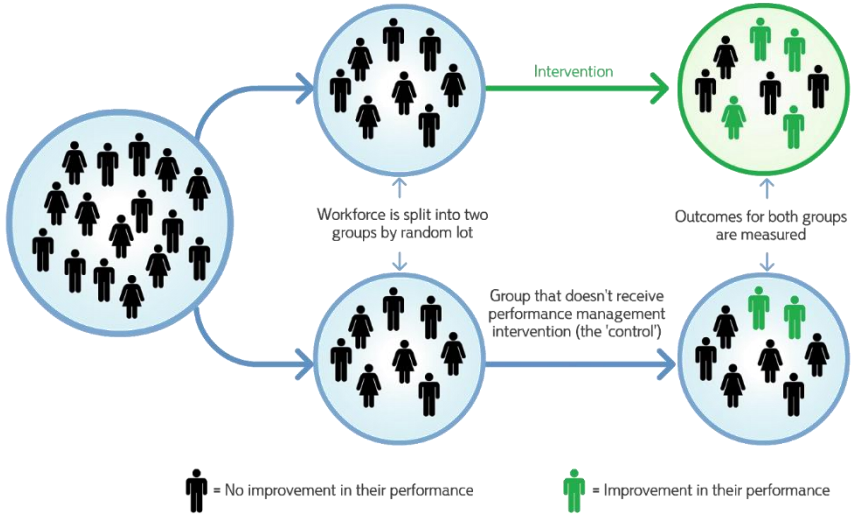
ALK = Anaplastic lymphoma kinase

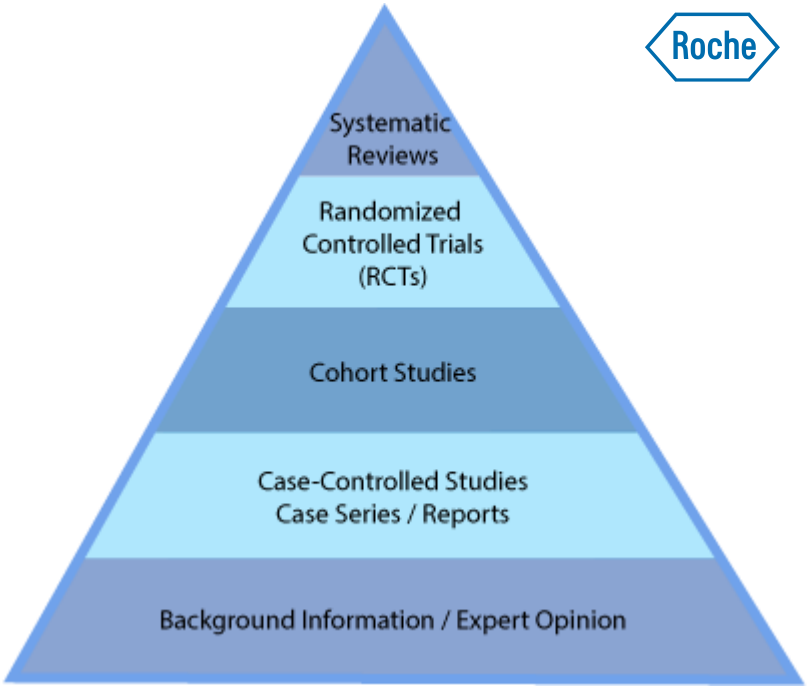
If a breast cancer patient with metastatic disease, had progressed on standard therapy, and then you found that she had an ALK mutation…

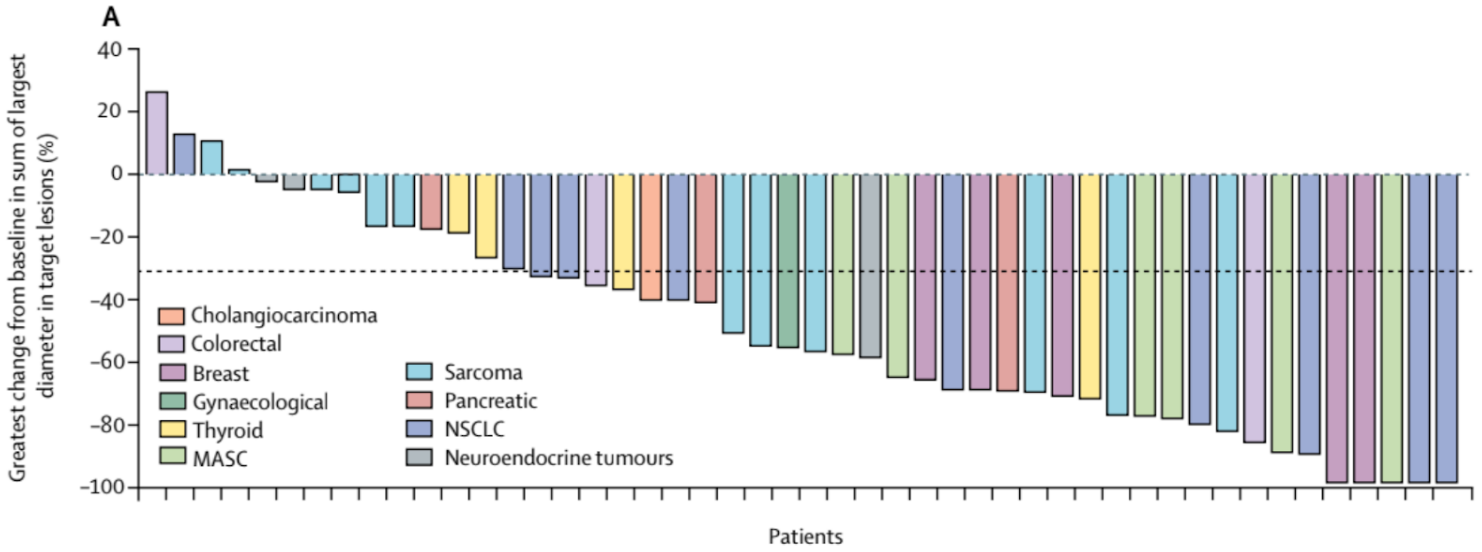
ALK = Anaplastic lymphoma kinase

Roche



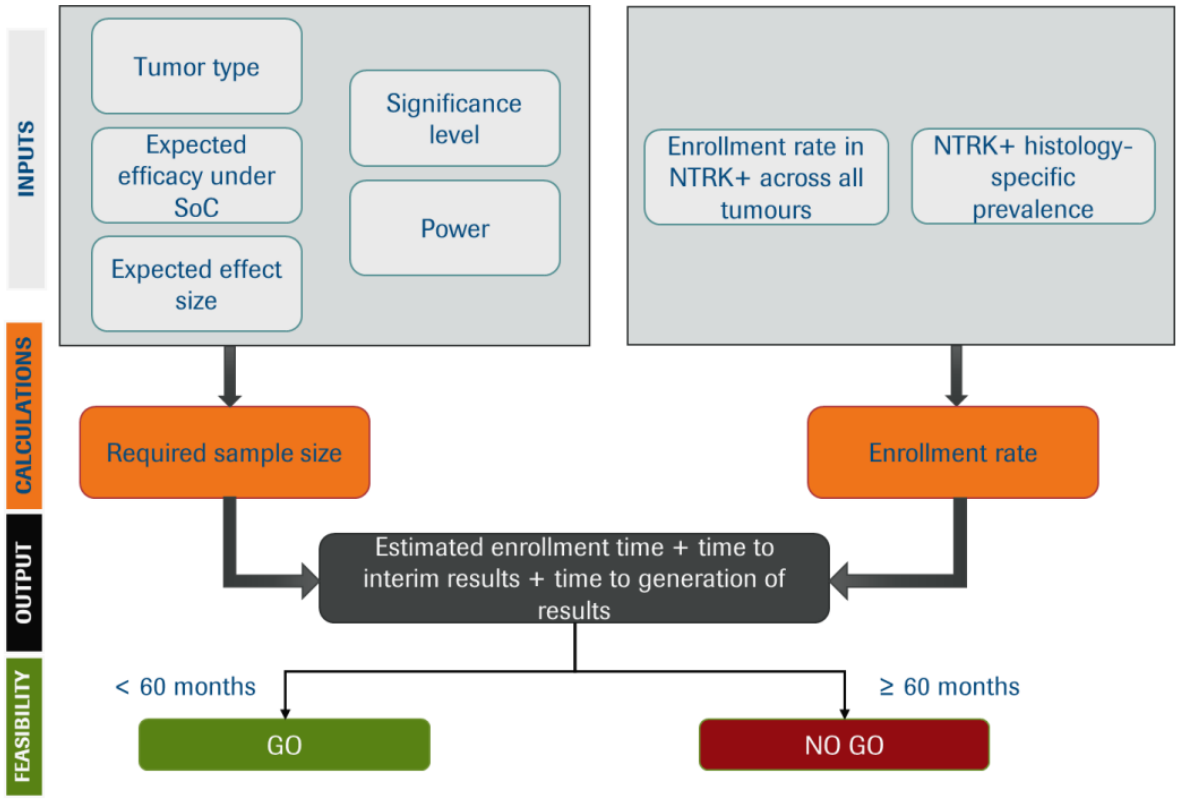






https://libguides.studiecentra.han.nl/Cochrane/beoordelingsformulieren

Are tumour specific RCTs feasible in indications with a low prevalence?



Sample size - related parameters

- The assumed primary outcome of interest was progression-free survival (PFS). The required sample size was estimated for each tumour based on the assumption of SoC PFS as reported for relevant SoC therapies (**Table 1**), and a clinically-meaningful difference of 30% reduction in PFS hazard associated with targeted therapy (1:1 allocation; alpha = 0.05; beta = 0.2).[2]
- Estimates of PFS at the tumour level were obtained from the literature from clinical trials of therapies prescribed in Canada for the management of patients with similar treatment experience in the STARTRK trial (NTRK+ patients).[1]

Enrollment rate - related parameters

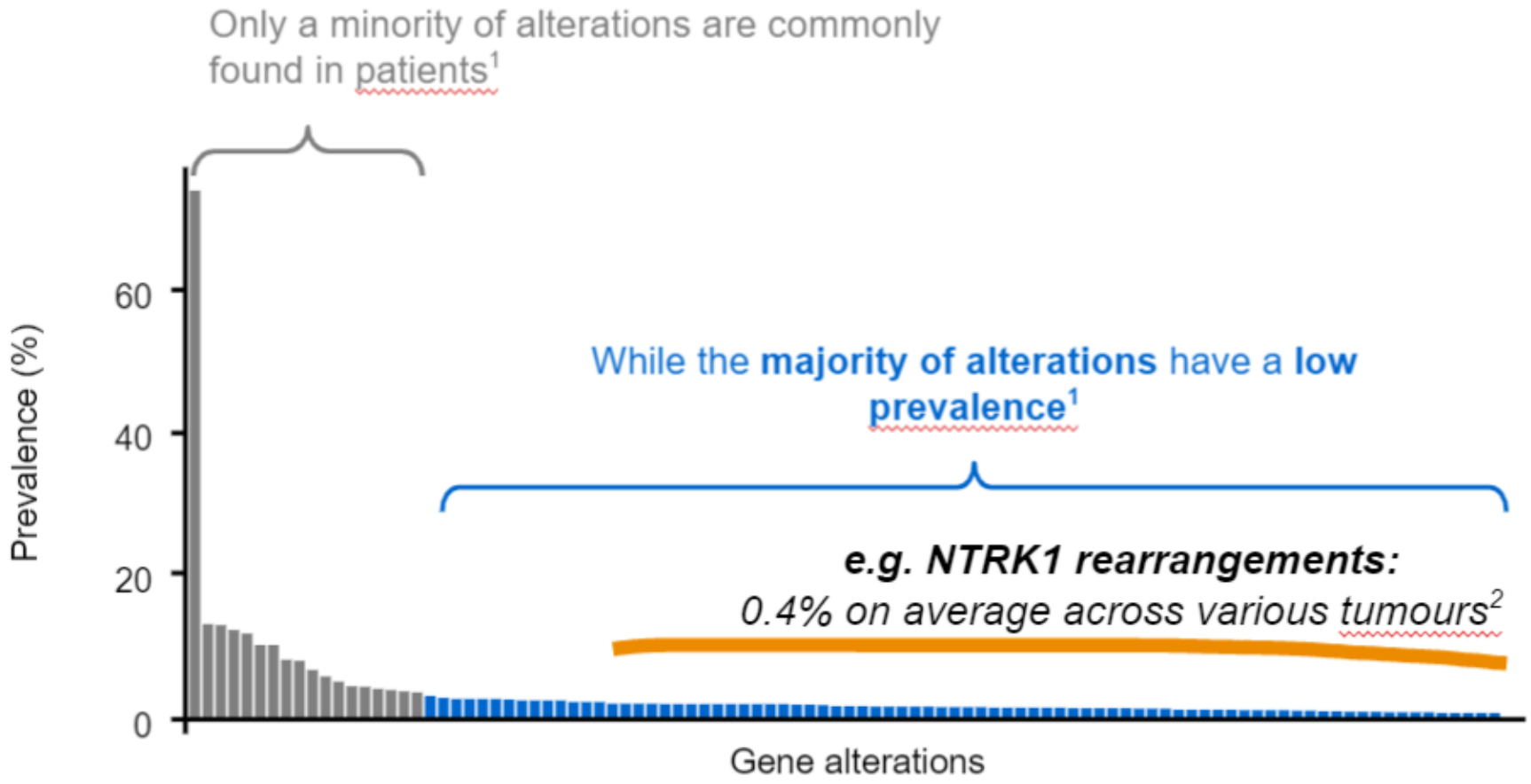
- Enrollment rate in each tumour-specific trial was dependent on the enrollment rate in the clinical trial program of NTRK mutations (STARTRK-2 2018 average; 4.25 patients per month over 150 sites).
- Patient enrollment across tumour-specific trials was assumed to follow the same distribution as observed in the STARTRK trial program (**Table 1**).
- The time required to enroll patients into each tumour-specific RCT was estimated based on the tumour-specific enrollment rate and the estimated sample size.

	Minimum sample size	Time to study results (years)	Feasible?
Colorectal cancer	215	55	✗
MASC	207	31	✗
Papillary thyroid	255	87	✗
Anaplastic thyroid	206	104	✗
Squamous NSCLC	206	104	✗
Non-squamous NSCLC	206	27	✗
Pancreatic cancer	206	70	✗
Sarcoma	209	17	✗
Neuroendocrine	222	76	✗
Secretory breast cancer	207	53	✗
Non-secretory breast cancer	207	105	✗

MASC: Mammary analogue secretory carcinoma; NSCLC: non-small cell lung cancer.

Lozano-Ortega, ISPOR poster 2019

The majority of alterations have a low prevalence, although often a high response rate to targeted medicines



Broad molecular profiling is necessary to reveal all possible relevant genomic alterations

Illustrative purposes only.

PHC: personalised healthcare; RWD: real-world data.

The number of regulatory approved tumour agnostic treatments is expected to grow exponentially

1. Data on File. FMI data base query; 2. Gatalica, Z., et al. (2019) *Mod Pathol* 32:147–53;

The challenge…

Regulatory approval ☑

≠

Reimbursement !

≠

Patient Access
(identification of patients)

HTA challenges and ways forward

Challenges

Ways forward

- **Level of knowledge & acceptance of precision oncology trial design**
  - **Outcome measures**
  - **Comparators**
  - **Small (often new) populations**

HTA challenges

Challenges

- Lack of knowledge and acceptance of precision oncology trial design
  - Other outcome measures
  - Relative effectiveness difficult
  - Small (often new) populations
- Evidence pack does not fit in the HTA assessment framework
  - Clinical benefit assessment on population level
  - How to deal with uncertainty?
    - Outcomes based pricing?
    - Pay for proof?

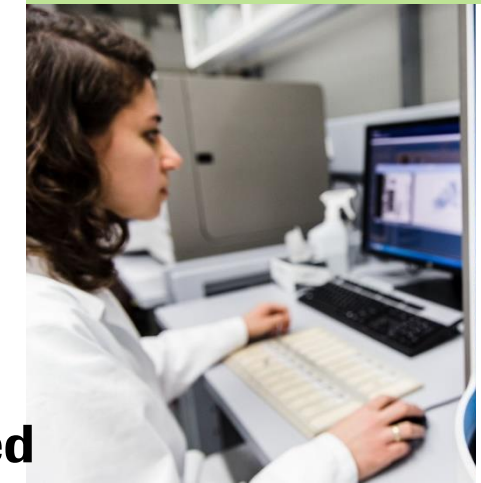
Ways forward

HTA challenges

Challenges

- Lack of knowledge and acceptance of precision oncology trial design
  - Other outcome measures
  - Relative effectiveness difficult
  - Small (often new) populations
- Evidence pack does not fit in the HTA assessment framework
  - Clinical benefit assessment on population level
  - How to deal with uncertainty?
    - Outcomes based pricing?
    - Pay for proof?
- No structural real world data collection for testing and outcomes
  - Identification of patients (for trials and registered therapies)
  - Unknown prognostic value of alterations
  - No learning system (now one off yes/no)

Ways forward



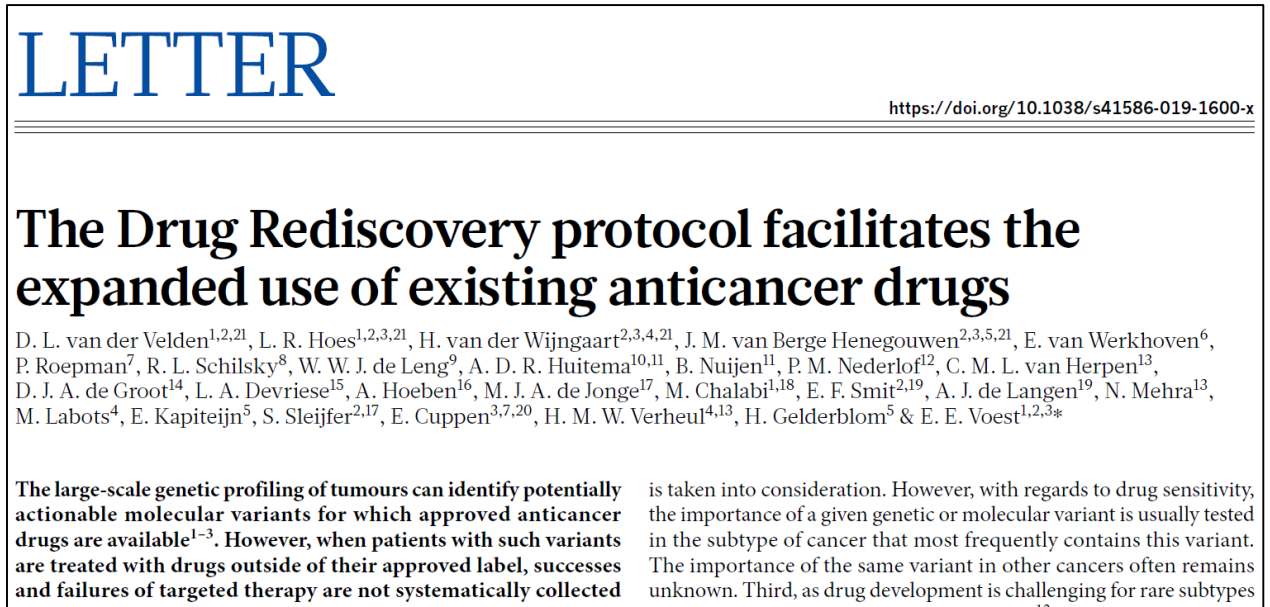
Creating system solutions takes time,
therefore the a temporary solution is being created

DRUP (Drug Rediscovery Protocol) a Dutch platform for medical oncologists to prescribe and monitor off-label treatments based on molecular alterations

DRUP

- *Collect RWD and provide access*
- *Personalized reimbursement model*

- Patients that exhausted SoC
- Additional treatment (MGTO)
- Off-label indications



LETTER

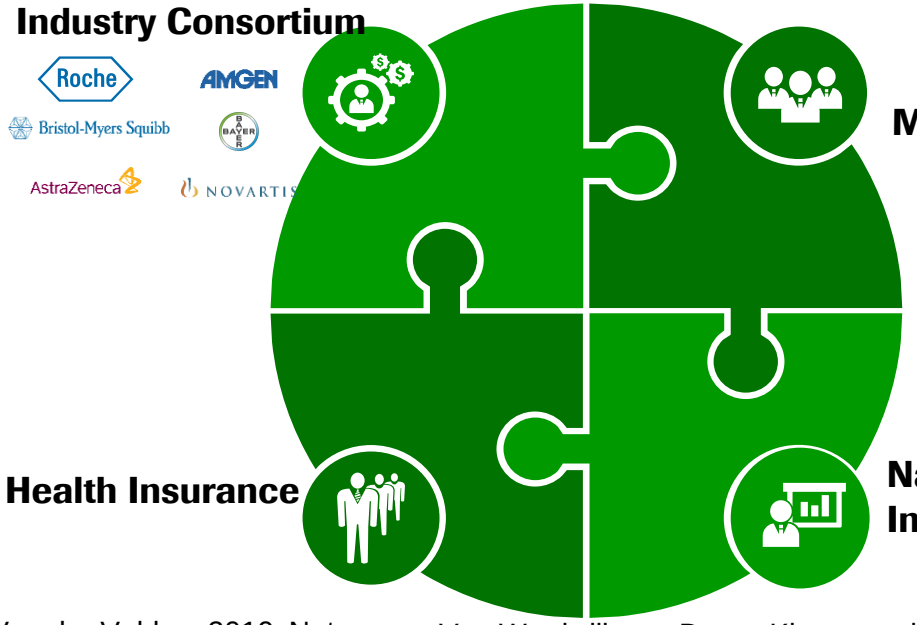
https://doi.org/10.1038/s41586-019-1600-x

The Drug Rediscovery protocol facilitates the expanded use of existing anticancer drugs

D. L. van der Velden[1,2,21], L. R. Hoes[1,2,3,21], H. van der Wijngaart[2,3,4,21], J. M. van Berge Henegouwen[2,3,5,21], E. van Werkhoven[6], P. Roepman[7], R. L. Schilsky[8], W. W. J. de Leng[9], A. D. R. Huitema[10,11], B. Nuijen[11], P. M. Nederlof[12], C. M. L. van Herpen[13], D. J. A. de Groot[14], L. A. Devriese[15], A. Hoeben[16], M. J. A. de Jonge[17], M. Chalabi[1,18], E. F. Smit[2,19], A. J. de Langen[19], N. Mehra[13], M. Labots[4], E. Kapiteijn[5], S. Sleijfer[2,17], E. Cuppen[3,7,20], H. M. W. Verheul[4,13], H. Gelderblom[5] & E. E. Voest[1,2,3]*

The large-scale genetic profiling of tumours can identify potentially actionable molecular variants for which approved anticancer drugs are available[1–3]. However, when patients with such variants are treated with drugs outside of their approved label, successes and failures of targeted therapy are not systematically collected

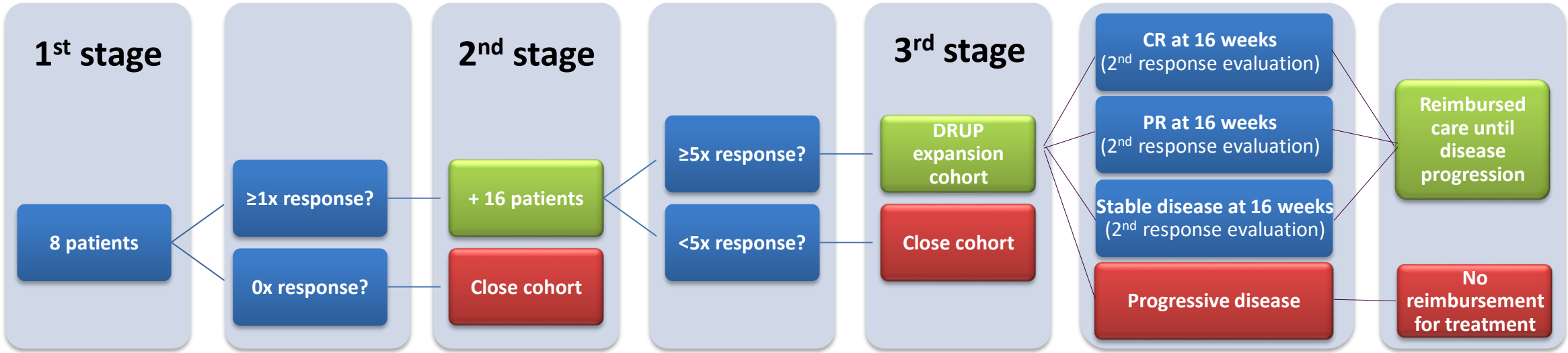
is taken into consideration. However, with regards to drug sensitivity, the importance of a given genetic or molecular variant is usually tested in the subtype of cancer that most frequently contains this variant. The importance of the same variant in other cancers often remains unknown. Third, as drug development is challenging for rare subtypes



Van der Velden, 2019, Nature

Van Waalwijk van Doorn-Khosrovani, 2019, Annal of Oncology

Stages in the Drug Rediscovery Protocol– study design per cohort



Van der Velden, 2019, Nature

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DRUP (Drug Rediscovery Protocol) and DAP (Drug Access Protocol) are two similar protocols with a different purpose

Key distinguishers

DRUP

- Collect RWD and provide access
- Personalized reimbursement model

- Patients that exhausted SoC
- Additional treatment options
- Off-label indications

DAP

- Collect RWD and provide access
- Personalized reimbursement model

- Type of evidence does not fit assessment frame
- On-label indications pre- and post registration

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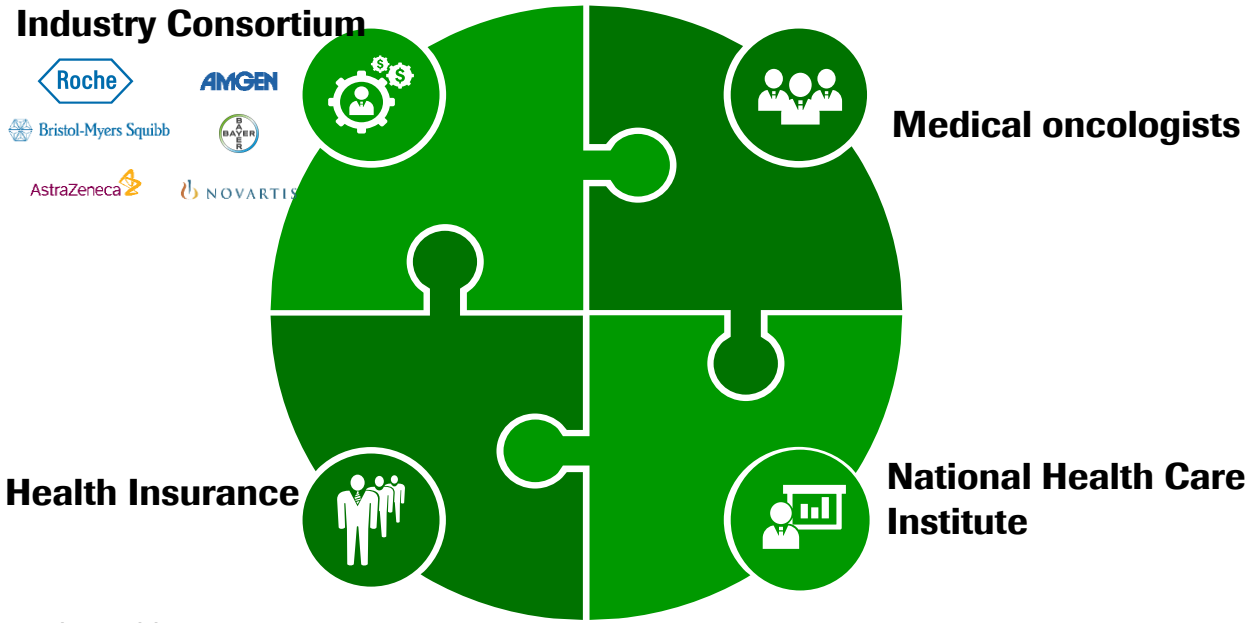

Van der Velden, 2019, Nature

Van Waalwijk van Doorn-Khosrovani, 2019, Annal of Oncology

Important steps… still miles to go

- Important steps are being set to bridge the gap between regulatory approval and reimbursement in the Netherlands.
- Stakeholders take responsibility to realize a future proof HTA and reimbursement system
- We’re not there yet, still work in progress

High quality, diagnostics for every cancer patient

National genomics/-omics data (knowledge) centre

National tumour board & shared decision making

Access to personalised treatment

Based on tumour profile, medical measures and the wishes of the patient

Automated collection of outcomes data to allow continuous learning

Payment for treatments based on outcomes/value

Roche

Doing now what patients need next

Thank you for your attention