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“Bringing innovative therapies to patients the NGS paradigm in routine diagnostics

Marc Van den Bulcke

Talinn 18 october 2017

WIV-ISP – Belgian Cancer Centre

NGS: Added value to current molecular diagnostics

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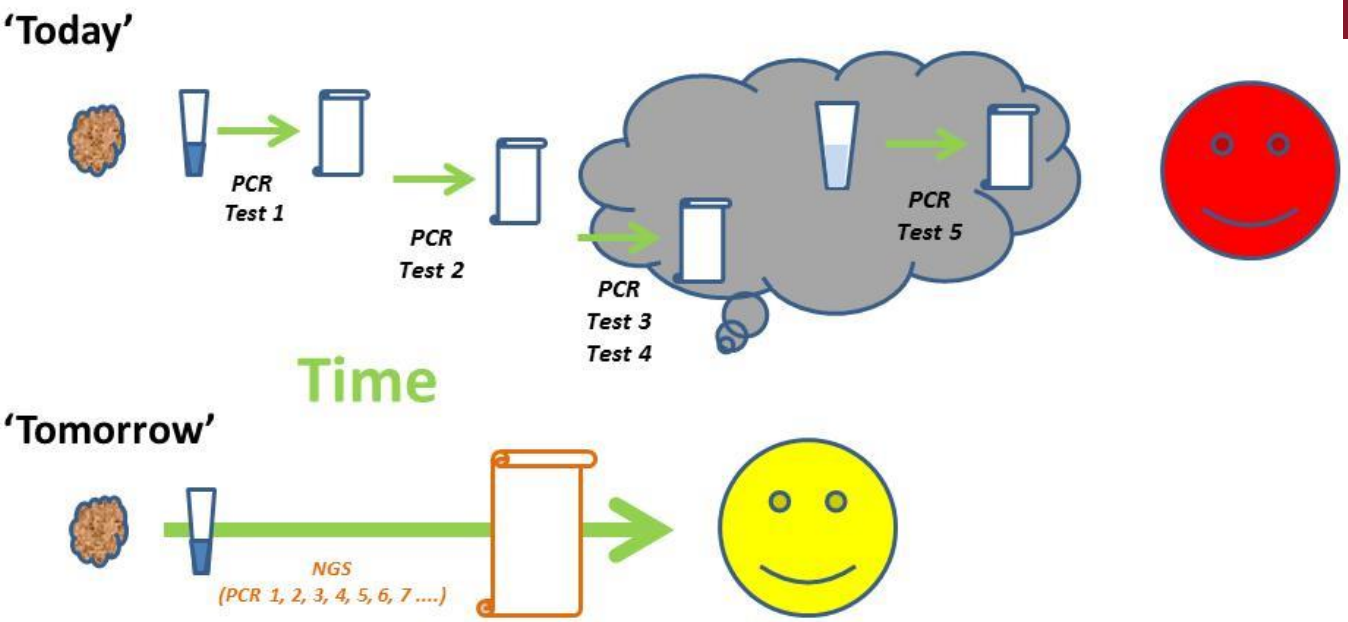

Advantages:

- ***Less*** material for ***more*** info
- Info at the DNA sequence level (***precision*** higher)
- Parallel analysis, ***faster*** conclusive results

Disadvantages:

- ***New*** paradigm (privacy, legal, ethical aspects)
- Major primary ***investment***
- ***Complex*** interpretation
- Does ***not substitute*** for all molecular testing (e.g. translocations)

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KCE
Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

NEXT GENERATION SEQUENCING GENE PANELS FOR TARGETED THERAPY IN ONCOLOGY AND HAEMATO-ONCOLOGY

MARC VAN DEN BULCKE, LORENA SAN MIGUEL, ROBERTO SALGADO, ELS DE QUECKER, HARLINDE DE SCHUTTER, ANOUK WAEYTENS, PETER VAN DEN BERGHE, SABINE TEJPAR, JEROEN VAN HOUDT, STEVEN VAN LAERE, BRIGITTE MAES, FRANK HULSTAERT

19 March 2015

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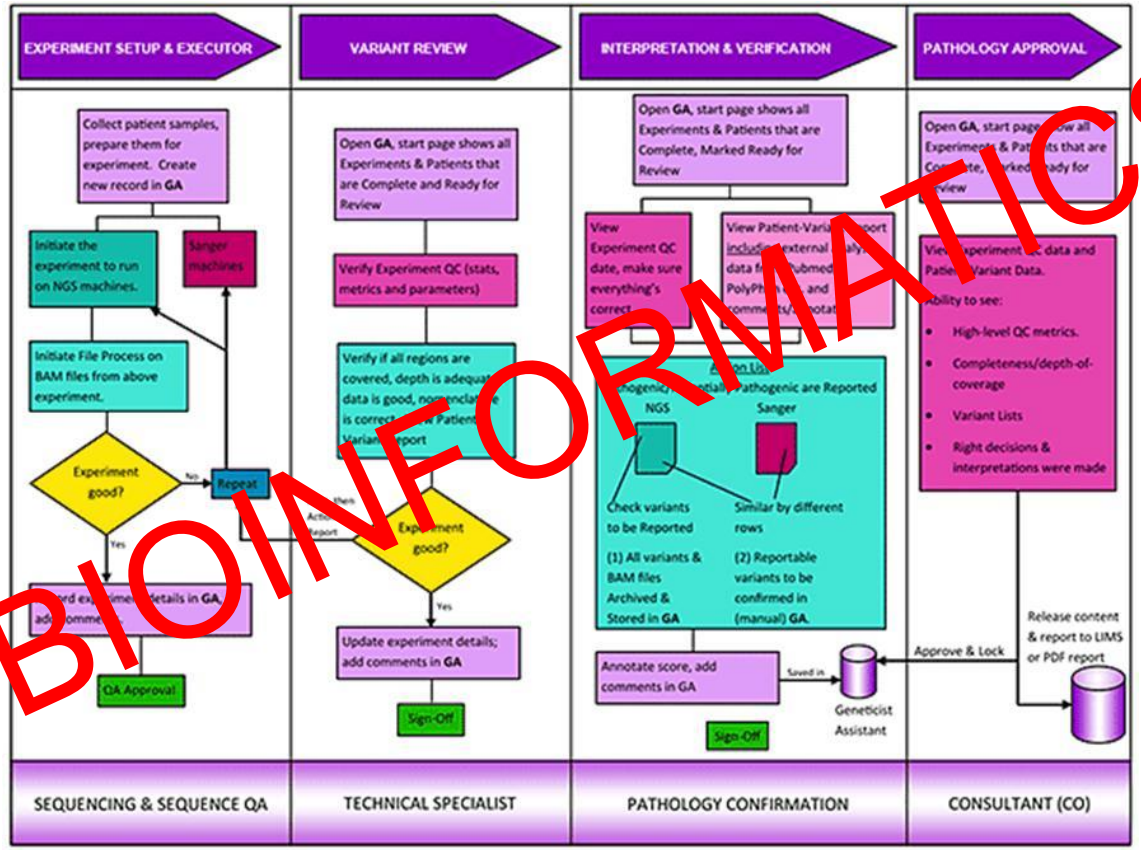

BIOINFORMATICS

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BRUSSEL, ***26/01/2016***.- Maggie De Block, minister van Volksgezondheid en Sociale Zaken, heeft in de commissie Volksgezondheid in de Kamer vandaag, 26 januari , benadrukt dat het **Kankerplan** wordt voortgezet met een reeks nieuwe maatregelen waaronder het **project "Next Generation Sequencing"** of NGS.
Bij NGS worden fragmenten erfelijk materiaal van het DNA getest om de kenmerken van een tumor of kanker te bepalen en die kenmerken geven aan welk geneesmiddel werkzaam zal zijn en welk niet. Patiënten zullen dus veel sneller dan vroeger een geneesmiddel kunnen krijgen dat werkt in hun specifiek geval.

BRUXELLES, ***26/01/2016***.- Maggie De Block, ministre de la Santé publique et des Affaires sociales, a souligné aujourd'hui, le 26 janvier, au sein de la commission santé de la Chambre que le **Plan Cancer** se poursuit à l'aide d'une série de nouvelles mesures, dont **le projet "Next Generation Sequencing" (NGS).**
Le NGS consiste à tester des fragments du matériel génétique de l'ADN afin de déceler les caractéristiques d'une tumeur ou d'un cancer. Ces caractéristiques détermineront quel médicament sera efficace ou pas. Les patients recevront donc bien plus vite qu'avant un médicament spécifiquement adapté à leur cas.

Roadmap 2016-2020 for 'NGS in routine analysis in oncology and heamato-oncology'

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- **Linkage CTG ΦTGR (drugs Φ tests)**
- **Expert WG on clinical utility of somatic mutations in oncology/heamato-oncology**
- **NGS guidelines and NGS gene lists**
- **Real-life pilot study**
  - Benchmarking test (2016/2017)
  - Real-life pilot study (2018-2020)
- **Data management (actionable mutations, reimbursement, register)**
- **Informed Consent (ethical and legal concerns)**
- **Education and training**

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“Commission on Personalized Medicine”

(December 2015)

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RIZIV - INAMI

Reimbursement for CDx – targeted therapies platform CTG-TGR

(December 2015)

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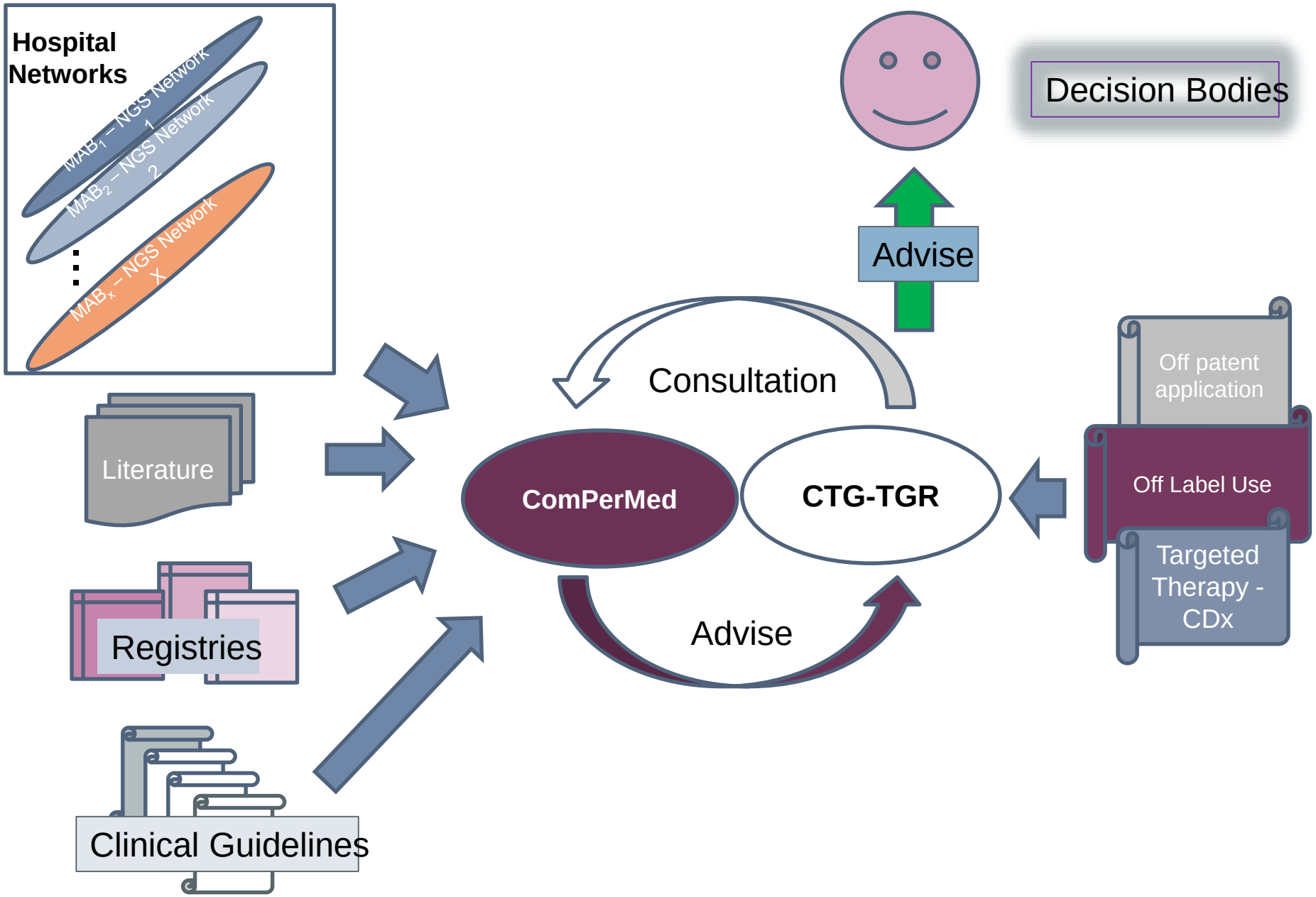
Hospital Networks
MAB1 – NGS Network 1
MAB2 – NGS Network 2
MABx – NGS Network X
Literature
Registries
Clinical Guidelines
ComPerMed
CTG-TGR
Consultation
Advise
Advise
Decision Bodies
Off patent application
Off Label Use
Targeted Therapy - CDx

Oncology Diagnostics

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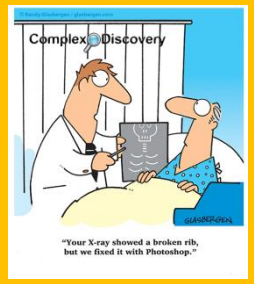
INTAKE



CANCER?

Imaging

Surgery
BIOPSY

Immuno
Q & RT-PCR
digPCR
Micro-array
FISH/ISH
Sanger seq
NGS
…

BioMol Reg

Molecular diagnostics

Test dbase
(auth.bron)

Cancer register
Incidence date

CYTOLOGY
HISTOLOGY

Cyto-Histo Reg

Pathology

OZG Reg

MOC

Treatment
CLINICIAN

Precision reg

Define NGS Guidelines for Oncology

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"The Belgian next generation sequencing guidelines for haematological and solid tumours" A. Hebrant et al., 2017 (in BJMO)

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NGS oncology diagnostics

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Selection of genes with a **clinical utility** for a specific indication

clinical utility

1. →To define **diagnosis**
2. → **Therapeutic** (To predict **sensitivity** or **resistance**)
3. → To determine **prognosis** for patient outcome.

→ **Levels of evidence**

NGS Gene panels and algorithms for solid and hematological tumors

NGS oncologic diagnostics

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Levels of evidence (UPDATED proposal by Cancer Center)

Level 1

- Standard of care biomarker for diagnosis and/or prognosis
- Biomarker predictive of a response or a resistance to a reimbursed drug in Belgium for this indication

Level 2

A

- Recommended standard of care biomarker for diagnosis and/or prognosis
- Biomarker predictive of response or resistance to an EMA-approved drug for this indication

B

- Biomarker predictive of response or resistance to a reimbursed drug in Belgium for another indication (clinical trial available in Belgium or EU)

Level 3

- Compelling clinical evidence supporting the biomarker for diagnosis and prognosis
- Biomarker predictive of a response or a resistance to
  - a non EMA-approved drug in this indication
  - a reimbursed drug in Belgium for another indication (clinical trial not available in Belgium or EU)
  - an EMA-approved drug for another indication
- Compassionate use

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Level 1 and Level 2A genes

CRC	BRAF KRAS NRAS		+
Pancreatic	GNAS BRCA1 BRCA2		+
Lung	BRAF KRAS EGFR ERBB2		+
Ovary/endometrial	BRCA1 BRCA2		+
Soft tissue sarcoma	Gist KIT PDGFRA		+
Brain	IDH2 IDH1	IDH2 H3F3A IDH1	Meduloblastoma panel +
Prostate	ATM BRCA1 BRCA2		+
Melanoma	BRAF KIT NRAS	uveal: GNAQ GNA11	+

PRELIMINAR

NGS oncology diagnostics

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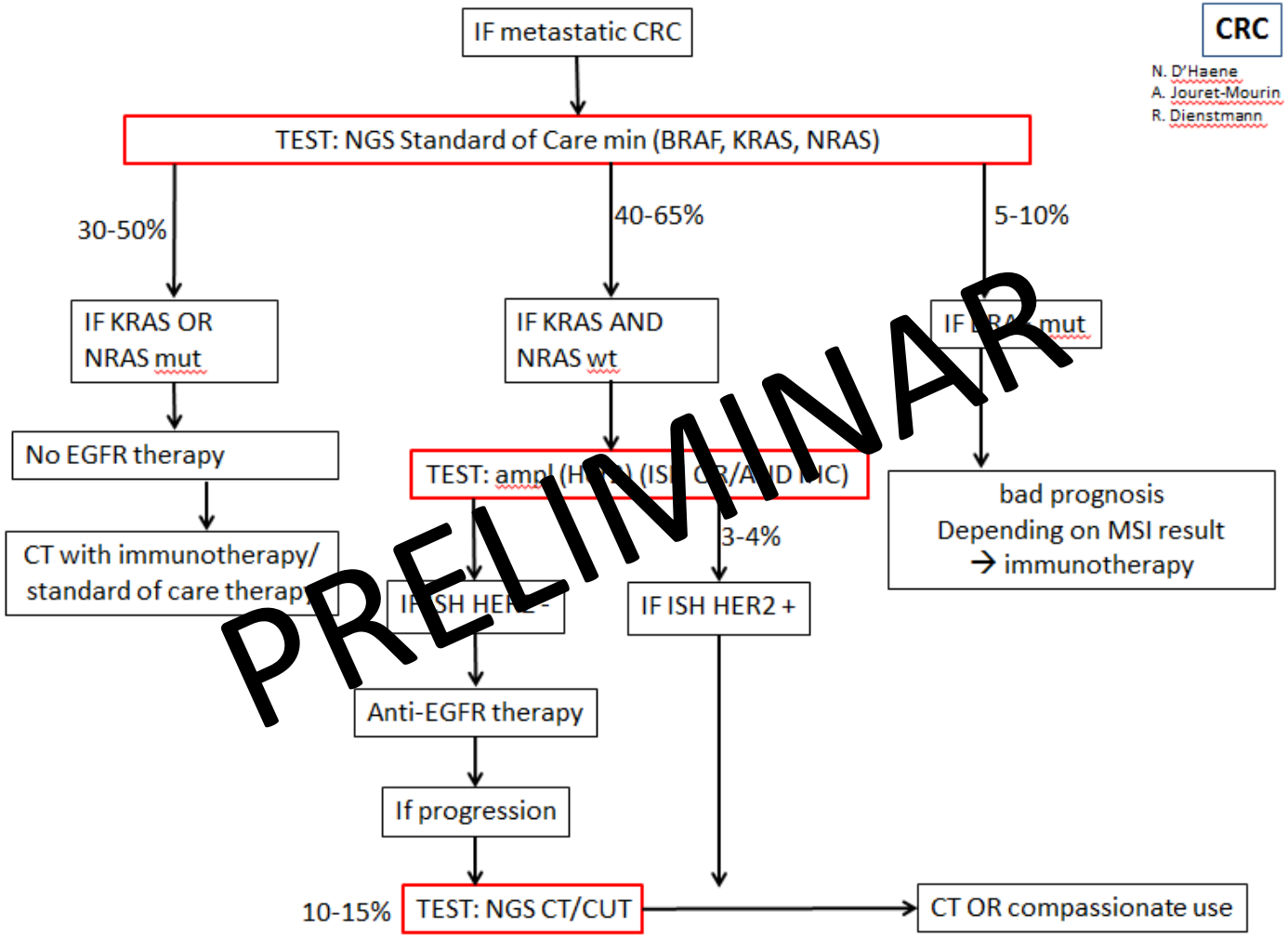
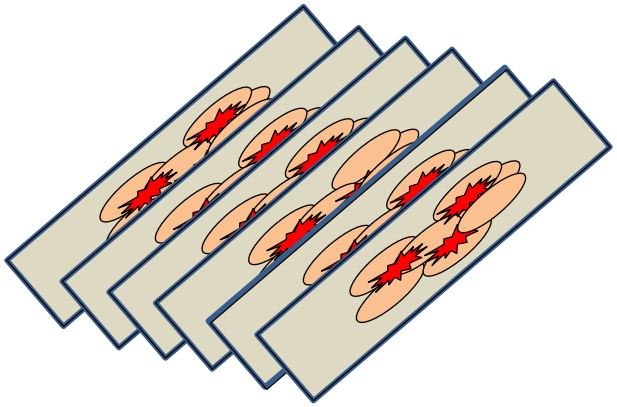
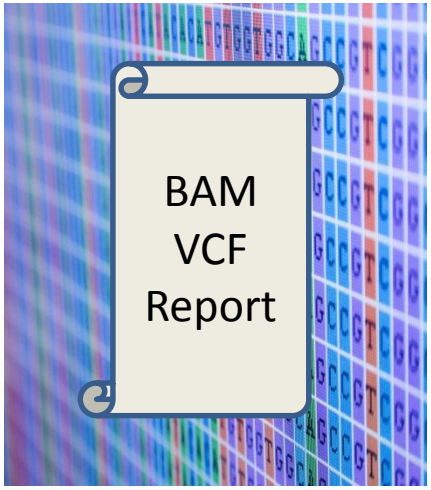
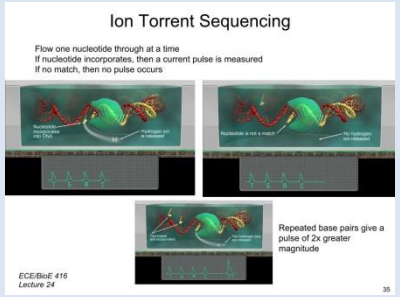
CRC's testing algorithm

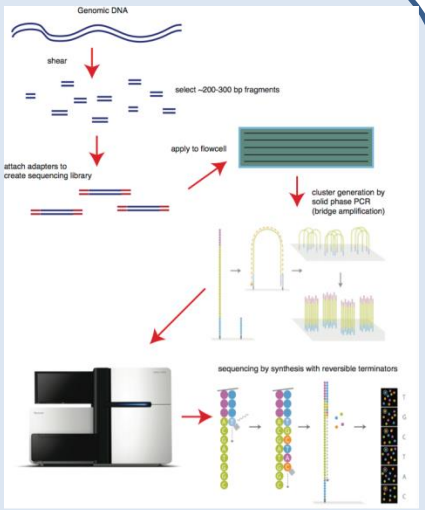


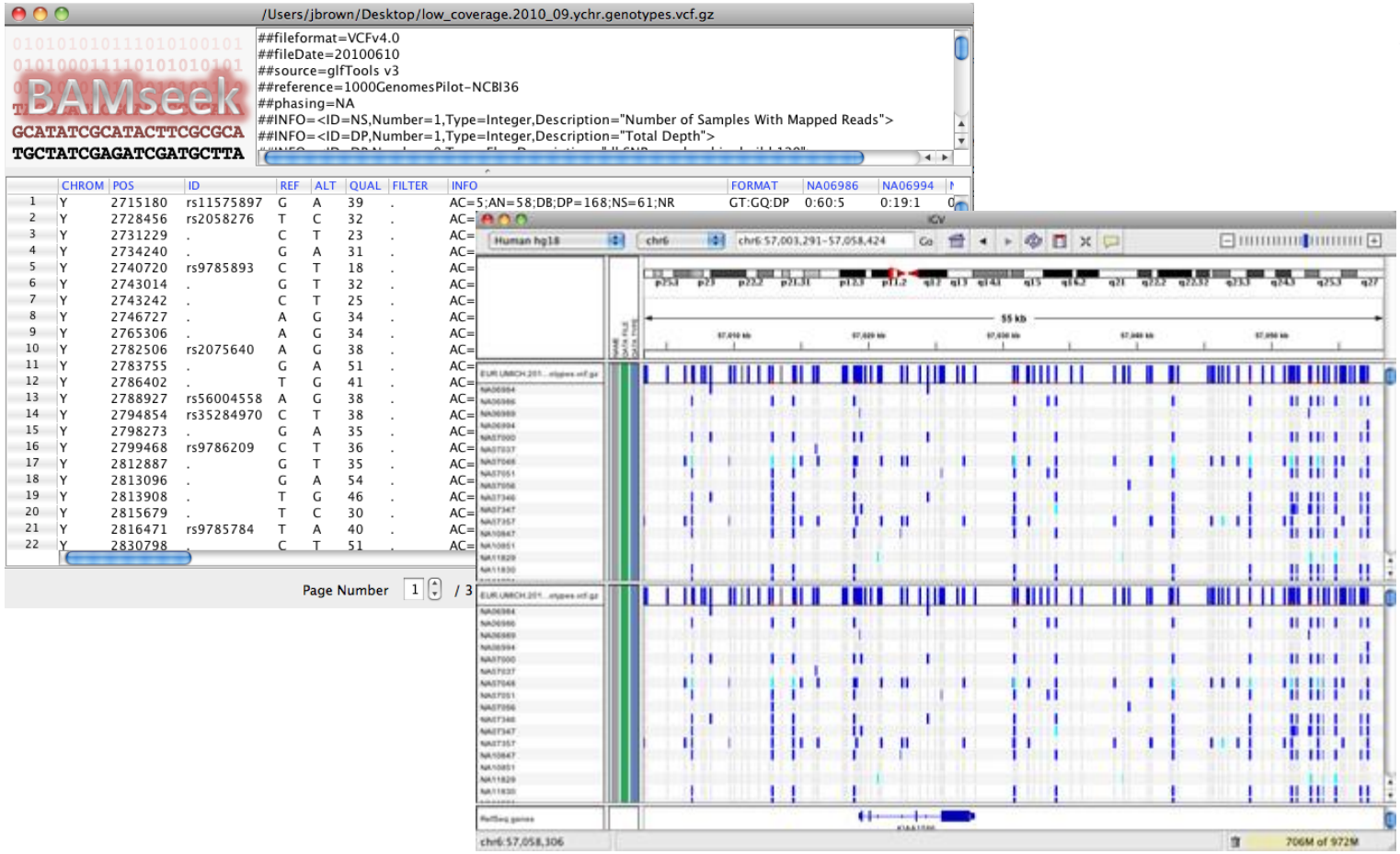
QA/QC: BENCHMARKING TRIAL (2017/2018)







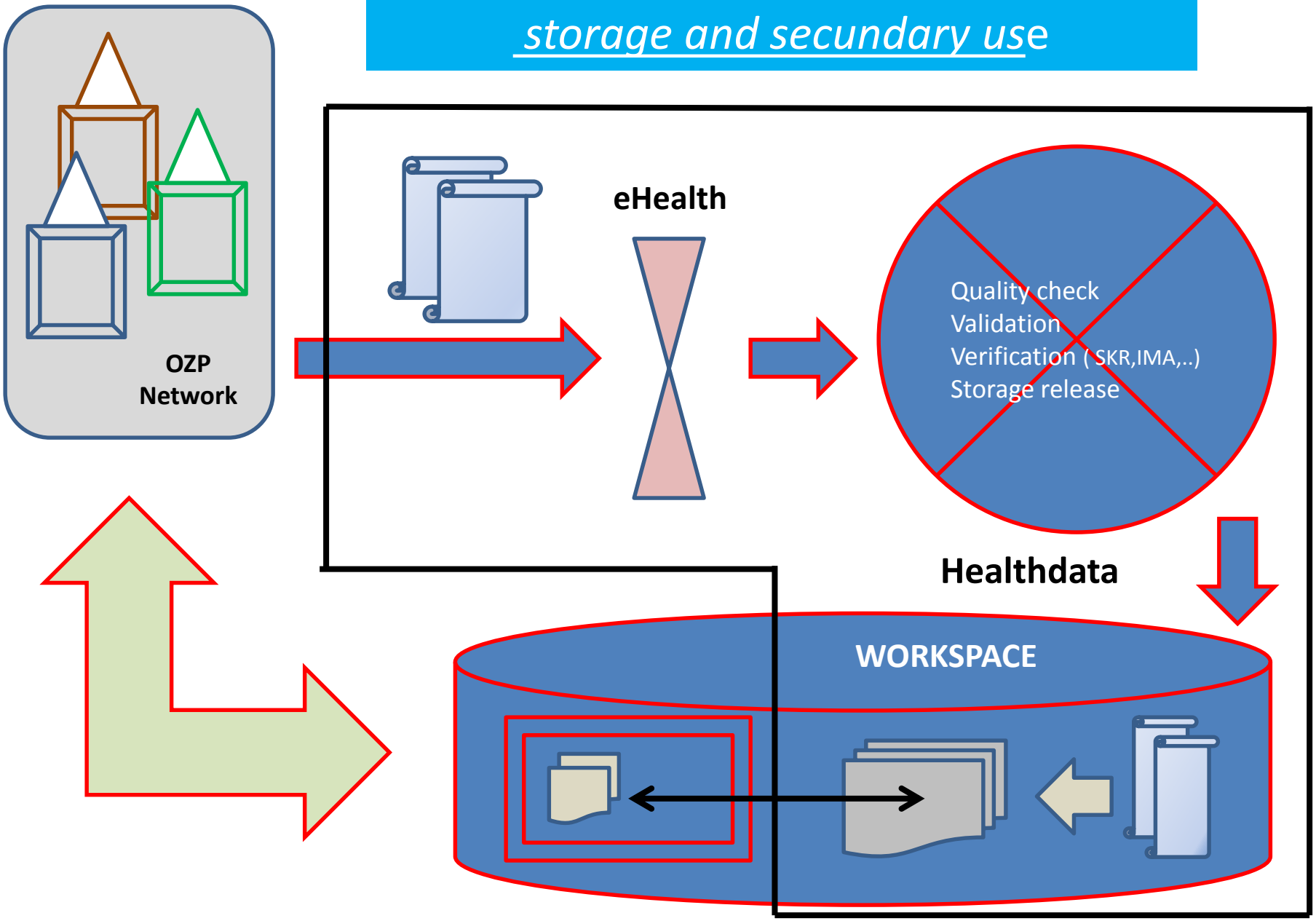




NGS Data registration

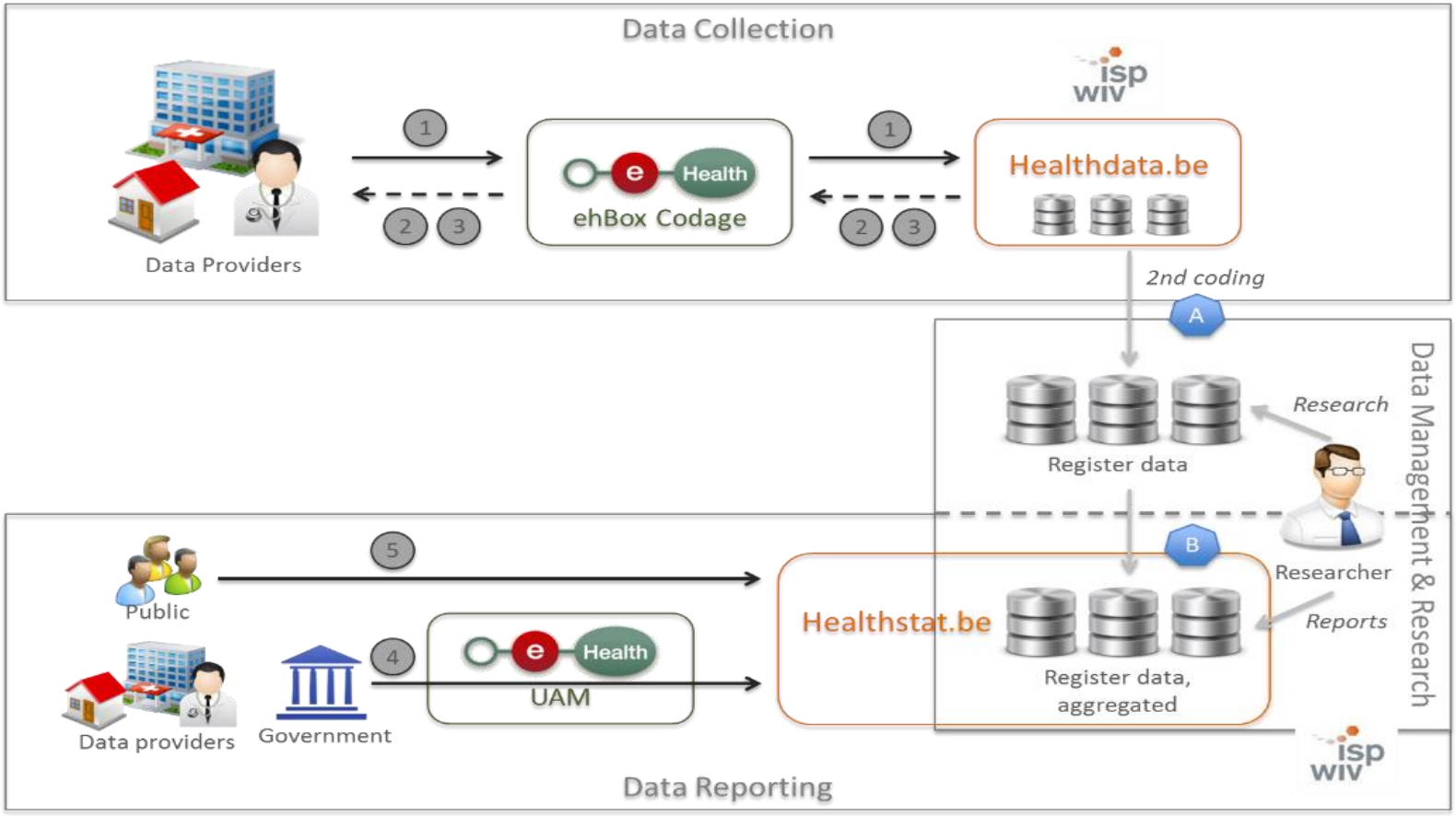
WIV-ISP Healthdata & Belgian Cancer Registry

Cancer NGS data registration, storage and secundary use



Healthdata NGS flow

Figuur 1: Algemeen overzicht gegevensstromen



EU initiatives

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- **Translational research at EC level:**

  Horizon 2020

  IC Permed consortium

- **Joint actions:**

  CanCon (end: Febr 2017)

  iPAACon Cancer (start in 2018)

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Treads and Opportunities

Challenge:

Quality of tests

Interpretation of results & Test algorithms - Reporting of data

Centralized data-registration

COST

Opportunity:

National EQA program

"ComPerMed "(Pathologists, Clinical Biologists, Oncologists, Geneticists, bioinformaticians,

National Healthdata register

(linked to CR for oncology)

Gene-panels with standard set of targets + variable part similar result interpretation tools

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THANK YOU

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