The NGS in (haemato)-oncology

Aline Hébrant, Els Van Valckenborgh, Marc van den Bulcke
Cancer Center

Standardize NGS technology in Belgium
– technical level and level of gene panel definition

1. The Belgian NGS guidelines for (haemato)-oncology

2. NGS gene panels for oncological use – solid tumors

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Goal | Methodology | Results | Perspectives

→ to **facilitate the implementation** of the NGS in the laboratories

→ to help lab to **generate accurate NGS data**

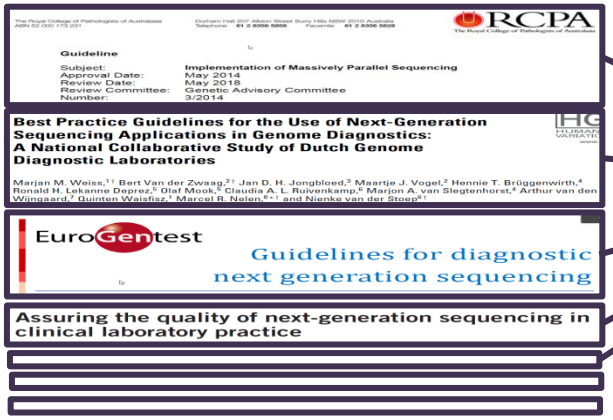
e.g. Identical sample analysis should lead to an identical list of variants even if processed by a different operator on a different day.

→ to **facilitate the evaluation by the auditors** from the accreditation bodies (Belac)

1. The Belgian NGS guidelines for (haemato)-oncology

Goal → Methodology → Results → Perspectives

1. Guidelines and publications (generally for genetics)



DRAFT:
NGS Belgian Guidelines

COMPLETED

2. 3 NGS guidelines meetings on 16th of February 2016, on 9th on March 2016 and on 10th of May 2016

COMPLETED

3. Many email exchanges and face to face meetings

COMPLETED

4. Final agreement by the scientific experts

COMPLETED

1. The Belgian NGS guidelines for (haemato)-oncology

Goal → Methodology → Results → Perspectives

5. Final approval by the ComPerMed management — **ONGOING**

→ **Final document: version 2016**

6. Published as a serie 7 by BELAC and submission to the peer-reviewed journal — **NEXT STEP**

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Goal | Methodology | Results | Perspectives

KCE report, March 2015

→ Importance to identify somatic mutations to personalize the treatments

→ A systematic methodology to define NGS gene panels which can be used in the oncological routine

→ to INAMI/RIZIV.

<u>WHY a new one?</u>

In commercial gene panels:

- Some genes included lack scientific evidence for their clinical utility
- Some genes with clinical utility are missing

2. NGS gene panels for oncological use

Goal | Methodology | Results | Perspectives

Concatenation of different gene panels:

From companies:

- Ion torrent: 50 genes
- Illumina: 48+ 54 genes
- Multiplicom: 26 genes

From National Institutes and Universities:

- INCA (Institut National du Cancer, France): 16 genes
- UCL-AD (University College London- UK): 22 genes
- SCRI (Sarah Cannon Research Institute, US): 35 genes
- CAP (College of American Pathologists, US):

  (when specified that the genes →clinically actionable)

  -UW Oncoplex (Pritchard) : 108 genes

  -Knight : 119 genes

  -ARUP laboratories : 88 genes

  -UPMC: 50 genes

From the Belgian experts: 206 genes

AZ St Jan (Brugge), AZ St Lukas (Gent), CHU Liege, IPG-Gosselies, Jessa_Hasselt, UCL, UZ Gent, LEUVEN, ULB (Bordet), Erasme, Antwerp, Histogenex, VUB (Brightcore), AZ delta (Roeselare)

Duplicates were removed

Solid tumor panel: 137 genes

Haemato tumor panel: 221 genes

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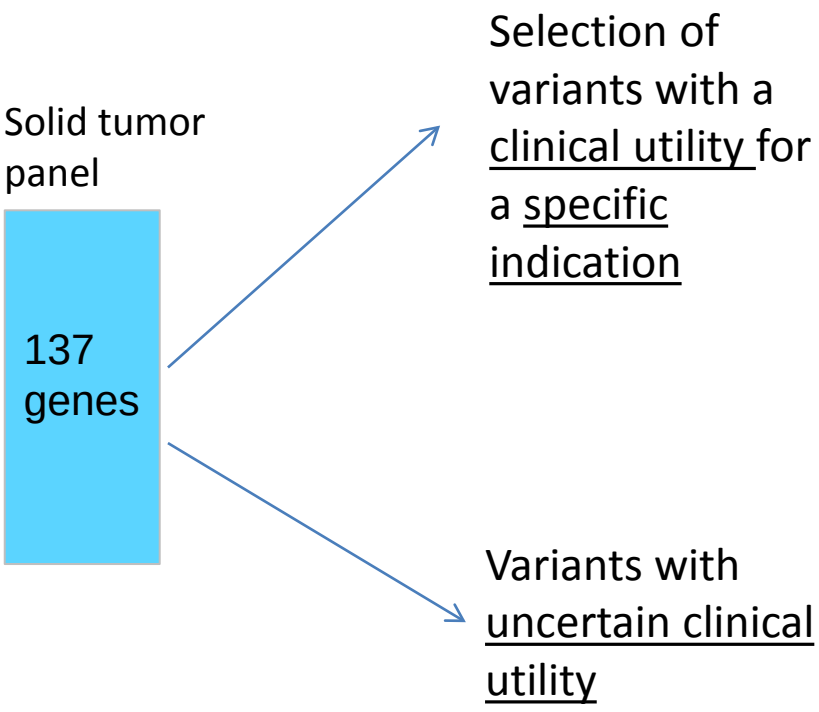

2. NGS gene panels for oncological use

Goal | Methodology | Results | Perspectives

→ The genes contained in the gene panel MUST have **a clinical utility:**

clinical utility

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

Genes included in the panel are either:

- Associated with a reimbursed cancer drug (Belgium, FDA, EMA)
- Present in clinical guidelines (e.g. CAP, BSMO, …)
- Tested in clinical trials (phase II & III)
- Reported in peer-reviewed scientific publications (review, article or communication)

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completer

→ **Level of evidence**

2. NGS gene panels for oncological use

Level of evidence (adapted from oncoKB)

Goal | Methodology | Results | Perspectives

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

- Recommended standard of care biomarker for diagnosis and/or prognosis
- Biomarker predictive of response or resistance to
  - a reimbursed drug in Belgium for another indication (clinical trial available in Belgium or EU)
  - an EMA-approved drug for this indication

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

2. NGS gene panels for oncological use

Level of evidence (adapted from oncoKB)

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2. NGS gene panels for oncological use

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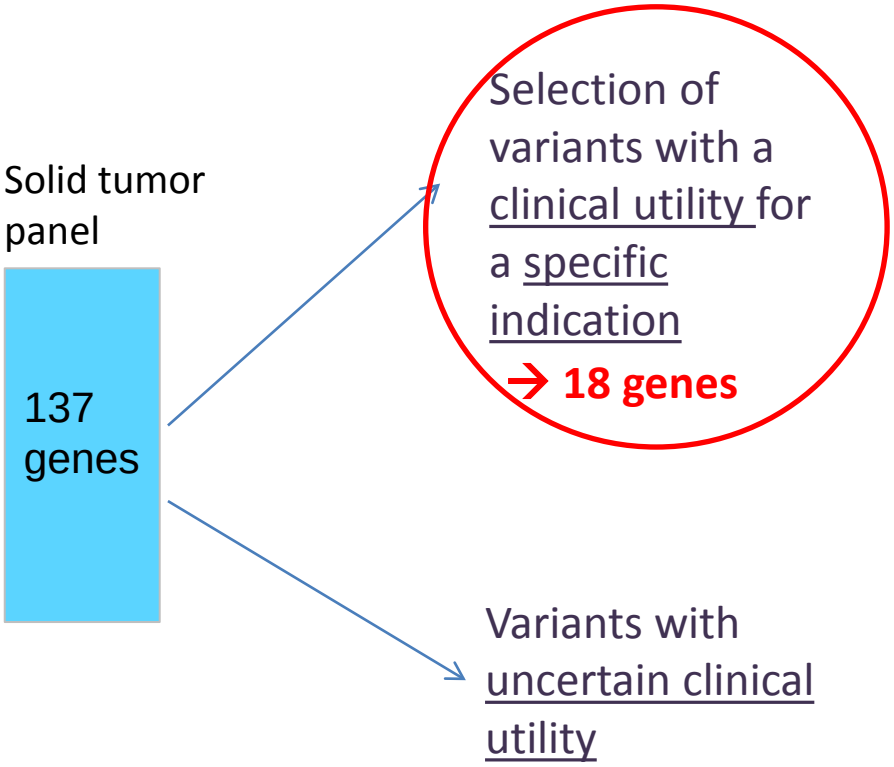

2. NGS gene panels for oncological use

Goal → Methodology → Results → Perspectives

Variants with a clinical utility for a specific indication

→ **18 genes**

1. Excel table:

For each gene in each tumor category (ICDO, WHO) :

- Mutation type (PM, ins, del)
- Clinical utility (Diagnosis, therapeutic, prognosis)
- Exons
- NM reference
- Sequence
- Level of evidence

2. Word document:

For each gene in each tumor category:

Scientific evidences:

- Clinical guidelines
- Reviews
- Scientific publications
- Clinical trials (phase 2 or 3)

2. NGS gene panels for oncological use

Goal → Methodology → Results → Perspectives

1. Excel table – 18 genes **COMPLETED**

tumor type	Gene name	Exons/codons	Tumor	Diagnostic	Prognostic	Therapeutic (Resistance/ Sensitivity/No Response)	NM
CRC							
	XXXX	exons X and Y	Colorectal cancer		X (2)	X (2)	NM_004
			Lynch syndrom/colorectal cancer	X (2)			
	YYYY	exons R	Colorectal carcinoma		X (1)	X (1)	NM_004
	ZZZZ	exons YY	Colorectal cancer			X(1)	NM_002
GIST							
	XXXX	exons Z				X (2)	NM_004
	AAA	exons D	GIST		X (3)	X (1)	NM_000
	TTTTT	exons FF	GIST		X (3)	X (1)	NM_006
Gastric							
Pancreatic							
	YYYY	exon T exon F	Mucinous carcinomas - pancreatic ductal adenocarcinomas (PDAs), pancreatic intraepithelial neoplasias mucinous cystic neoplasms (MCNs), neuroendocrine neoplasms cinar cell neoplasms, serous cystadenomas, solid-pseudopapillary neoplasms	X (2)			NM_000
	VVVVV	exons E	pancreatic cancer	X(2)		X (3)	NM_004

2. Meetings, many email exchanges and face to face meetings with the Belgian expert group: To decide the minimal required genes to be analyzed per tumor type. **ONGOING**

3. Same methodology with the haemato- oncology (Els Van Valckenborgh) **ONGOING**

→ Final proposition

4. Advice to the platform CTG/TGR of INAMI/RIZIV **NEXT STEP**