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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1. The Belgian NGS guidelines for (haemato)-oncology
2. NGS gene panels for oncological use – solid tumors
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**
Guidelines and publications (generally for genetics)

**Methodology**

**Results**

**Perspectives**

1. DRAFT: NGS Belgian Guidelines

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

3. Many email exchanges and face to face meetings

4. Final agreement by the scientific experts
1. The Belgian NGS guidelines for (haemato)-oncology

- Goal
- Methodology
- Results
- Perspectives

5. Final approval by the ComPerMed management

Final document: version 2016

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

ONGOING

NEXT STEP
The NGS in (haemato)-oncology
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2. NGS gene panels for oncological use

KCE report, March 2015

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

→ 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.

WHY a new one?
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

**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):
    - UW Oncoplex (Pritchard): 108 genes
    - Knight: 119 genes
    - ARUP laboratories: 88 genes
    - UPMC: 50 genes

**From the Belgian experts:**
- 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)
2. NGS gene panels for oncological use

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  - CAP (College of American Pathologists, US): (when specified that the genes \(\rightarrow\) clinically actionable)
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Solid tumor panel:
137 genes

Haemato tumor panel:
221 genes

Duplicates were removed
206 genes
2. NGS gene panels for oncological use

Goal

Methodology

Results

Perspectives

Solid tumor panel

137 genes

Selection of variants with a clinical utility for a specific indication

Variants with uncertain clinical utility
2. NGS gene panels for oncological use

→ 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)
2. NGS gene panels for oncological use

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**Level of evidence**
2. NGS gene panels for oncological use

Level of evidence (adapted from oncoKB)

Goal

Methodology

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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)

<table>
<thead>
<tr>
<th>Level 1</th>
<th>Level 2</th>
<th>Level 3</th>
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<tr>
<td>Goal</td>
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</table>
2. NGS gene panels for oncological use

Goal
Methodology
Results
Perspectives

Solid tumor panel
137 genes

Selection of variants with a clinical utility for a specific indication → 18 genes

Variants with uncertain clinical utility
2. NGS gene panels for oncological use

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

1. Excel table – 18 genes

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Tumor Name</th>
<th>minimal required genes</th>
<th>Analyzed genes</th>
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<tbody>
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<td>CRC</td>
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<td>X (3)</td>
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<tr>
<td>CCC</td>
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<td>X (2)</td>
</tr>
<tr>
<td>DDD</td>
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<td></td>
<td>X (2)</td>
</tr>
</tbody>
</table>

COMPLETED

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

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

NEXT STEP

Final proposition