WGS Implementation in standard cancer Diagnostics for Every cancer patient

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The WIDE project aims to investigate if implementation of WGS in molecular diagnostics is feasible in routine practice at the Netherlands Cancer Institute (NKI).

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON49090

Source
ToetsingOnline

Brief title
WIDE

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
Cancer, tumors

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: ZonMW,Hartwig Medical Foundation

Intervention

Keyword: Biomarker, Diagnostics, Personalized medicine, Whole genome sequencing

Outcome measures

Primary outcome

• Feasibility: The percentage of samples that successfully been processed from biopsy to WGS report in an acceptable turnaround time (2-3 weeks).

• Clinical validation: The percentage of samples for which WGS minimally reports the same treatment-relevant variants as SOC DNA diagnostics (e.g. next generation sequencing (NGS) panels, RNA-based NGS fusion analysis, Sanger sequencing, RT PCRs, and FISH)

• Health Technology Assessment of WGS as compared to SOC diagnostics.

Secondary outcome

• Additional treatment options: the percentage of patients for whom potential treatment options (in clinical trials) are identified by WGS that have not been identified using SOC diagnostic assays performed for this patient.

• Better informed decision making/experience of the treating physician: the opinion of treating physicians on the added value of WGS for decision making compared to SOC diagnostics. This will be evaluated with questionnaires for the treating physician and is a qualitative analysis.

• Expanding the HMF database: the number of patients whose clinical and WGS data is added to the HMF database

Study description

Background summary

By tailoring treatment towards individual patient and tumor characteristics using biomarkers that predict clinical efficacy, *precision oncology* can ensure each patient receives the right treatment at the right time. The rapid increase in the number of new biomarkers in oncology has led to a large variety of diagnostic platforms, such as targeted next generation sequencing (NGS) panels, RNA-based NGS fusion analysis, Sanger sequencing, RT-PCRs, FISH and IHC. All these platforms address a small part of the diagnostic spectrum and are often performed in an iterative way to reduce costs, however, at cost of valuable time and tissue. In addition, when new biomarkers are added, often another assay is added to this list or an existing test needs to be expanded and (re-)validated for the new biomarker, which takes a substantial amount of time and resources and complicates reporting.
We need a comprehensive diagnostic pipeline that optimally uses the available tumor tissue in an acceptable turnaround time. This comprehensive test needs to keep up with the pace of the rapidly changing current oncology landscape with respect to new biomarkers and clinical trials and should result in a comprehensive, yet comprehendible, diagnostic report.
Whole Genome Sequencing (WGS) is a next generation NGS technology that can map the complete genetic composition and practically all of the aforementioned biomarkers of a tumor in a single assay. WGS is efficient with respect to tissue-consumption, as it requires relatively low amounts of input material. Simultaneously, costs for WGS are steadily decreasing and therefore WGS is becoming an attractive alternative for standard molecular diagnostics. WGS thereby allows simplifying laboratory logistics with a *one-size-fits-all* test instead of multiple different stand-alone tests that need validation for every new indication.
Despite the potential of WGS, the actual value and feasibility in a routine diagnostic setting has not yet been demonstrated.

Study objective

The WIDE project aims to investigate if implementation of WGS in molecular diagnostics is feasible in routine practice at the Netherlands Cancer Institute (NKI).

Study design

observational diagnostic consecutive cohort study

Main objectives:
- stepwise confirm the feasibility of WGS in routine clinical cancer care;
- clinically validate WGS in a consecutive prospective diagnostic cohort in the NKI.
- compare the costs and benefits associated with WGS and the SOC pathology

diagnostics.

Secondary objectives:
- explore differences in the annotation and interpretation of variants using WGS reporting vs SOC reporting;
- identify additional potential treatment options revealed by WGS that cannot be identified using SOC diagnostic assays;
- explore the effect/benefit of WGS availability on the decision-making process by the treating physicians;
- expand the HMF database of clinically annotated and WGS analysed patients for future research purposes

Study burden and risks

- A fresh or fresh-frozen tumor material of the metastatic or primary lesion will be obtained as part of routine standard of care (SOC) diagnostic procedures. Tumor material means resection, biopsy or body fluid containing tumor cells, such as pleural fluid or ascites. In case of a biopsy, multiple tumor biopsies are obtained from all patients as part of the routine SOC diagnostic procedure. There will be no additional biopsy taken for WIDE, thus there will be no extra burden for the patient.
- A 10ml blood sample will be drawn once. This blood draw will by preference be done during a regular blood draw needed for routine care. The risk of a blood draw is negligible.
- Actionable (treatment-relevant) germline mutations (eg BRCA1 / 2) will be reported to the patient if the patient chooses to receive these findings. This can lead to information about hereditary predisposition to cancer, which may also have consequences for family members of the patient. The patient can indicate on the consent form whether she wants to be informed of these changes in the germline DNA.
- Results from WGS diagnostics will be used to support clinical decision making and care, which could identify additional treatment options. These subsequent therapies will be SOC or patients will be included in experimental studies: in regular clinical studies with experimental agents or in the Drug Rediscovery Protocol (DRUP), for all of which a separate informed consent will be asked. Therefore, no experimental intervention will be implemented in the current project and the workflow will parallel current diagnostic and treatment strategies.

Contacts

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Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• (suspicion of) stage IV disease from solid tumors;
• collection of tumor material (biopsy, resection, or body fluid containing tumor cells) can safely be obtained during routine diagnostic procedures;
• a routine diagnostic procedure in case of newly collected tumor material or routine molecular diagnostic procedure in case of fresh frozen archival tumor material or tumor material collected in the context of a research/translational study;
• treatment will be received at the Antoni van Leeuwenhoek;
• age 18 years or older, willing and able to comply with the protocol as judged by the investigator;
• written informed consent.

Exclusion criteria

• Age below 18 years;
• No metastatic disease or suspicion of metastatic disease;
• Archival tumor material of a patient who has received immune and/or targeted therapy after collection of tumor tissue;
• Prior participation in WIDE with a successful WGS analysis unless it concerns molecular analysis for resistance to tyrosine kinase inhibitors;
• Allogeneic stem cell transplantation or transplantation of the organ in which the tumor originated or is located

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-04-2019
Enrollment:	1200
Type:	Actual

Ethics review

Approved WMO

Date:	10-04-2019
Application type:	First submission
Review commission:	METC NedMec

Approved WMO

Date:	23-05-2019
Application type:	Amendment
Review commission:	METC NedMec

Approved WMO

Date:	21-08-2019
Application type:	Amendment
Review commission:	METC NedMec

Approved WMO

Date:	23-01-2020
Application type:	Amendment
Review commission:	METC NedMec

Approved WMO

Date:	11-06-2020
Application type:	Amendment
Review commission:	METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL68609.031.18