AGMT_NGS REGISTRY

The Use of Genomic Testing and the Resulting Medical Decisions According to Target Identification

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Protocol Synopsis

Indication: Patients for which broad genomic profiling is indicated as assessed by the medical need

Planned sample size: 500 – 1.000 patients

Recruitment: 360 patients as of March 2019

Design: Retrospective and prospective, multicenter, non-interventional, observational

Duration: Q1 2017 - Q4 2019

Planned amendment: Prolongation of study duration until Q4 2021 and increase the number of patients to 1.000

Rationale

In the situation of enormous possible beneficial options for patients, health care systems, researchers and companies and the simultaneously present high number of uncertainties, the establishment of an independent registry for patients undergoing any type of comprehensive genomic profiling offers many advantages.

There is no evidence available about which molecular profiling methods are currently used for cancer patients in Austrian clinical practice. The construction of the registry proposed as a completely independent research endeavor, will be helpful for scientific evaluation and the establishment of highly credible data.

The registry proposes to cover the time period from the years 2016 to 2019, which will allow for assessment of both the current and emerging landscape of genomic/molecular testing practice in Austria and effect of molecular profiling on patient care and outcome.

Study Design

This registry is designed as multicenter non-interventional (observational) cohort of oncology patients who received or plan to receive comprehensive genomic testing. Patient medical, testing and treatment information will be obtained through extraction of data from existing patient medical charts. Longitudinal follow-up data, including survival and tumor progression, will also be extracted from patient medical charts. This patient follow-up data will be obtained until patient death or loss to follow-up.

The registry will be made available for all disciplines and physicians caring for cancer patients. Indications for genomic testing are exclusively driven by the medical need. Physicians are free to use any type of genomic test available at their hospital or from any company. The decision to use comprehensive genomic testing must be clearly separated from the decision to include the patient in the registry.

Objectives

Primary objectives

To describe the distribution and types of:
- molecular profiling methods used in the Austrian registry centres
- cancer, for which comprehensive molecular profiling is used
- the timing of molecular profiling in relation to stage of the disease (e.g. at diagnosis, after surgery, radiation therapy, after first/second/third/late line)

Secondary objectives

To describe targets identified:
- number of patients with at least one mutation identified
- number of patients with at least one druggable target identified
- number of patients with more than one druggable targets identified
- number of druggable targets per cancer type
- usage of commercial testing vs. in-house testing, platforms used, and number of genes as well as gene size analyzed (eg whole exome with or without selected intron sequencing vs. hot spot exome sequencing)
- to evaluate patient outcome by means of overall survival (OS) and progression free survival (PFS)
- to investigate the alterations in patients, who are not responders to previous regimens/drugs (eg some alk+ lung cancer patients do not respond to treatment with 1st and 2nd generation alk inhibitors)
- compare PFS/OS/response with outcome of last treatment before genomic profiling

To describe tests used and quality standards:
- to compare results of NGS based molecular test systems with single marker tests or small gene panel tests
- quality standards of the test methods used (TAT, certification status)
- to evaluate development of methods used over time
- usage of commercial testing vs. in-house testing, platforms used, and number of genes as well as gene size analyzed (eg whole exome with or without selected intron sequencing vs. hot spot exome sequencing)

To describe treatment decisions:
- frequency by which treatment decision follows the result of NGS testing
- frequency with druggable targets with available on-label therapy option
- treatment decisions in the presence of more than one druggable target

To describe outcome of treatment in patients receiving therapy in concordance with the test result:
- frequency and degree of response
- treatment duration of the therapy following test result
- to evaluate patient outcome by means of overall survival (OS) and progression free survival (PFS)
- to investigate the alterations in patients, who are not responders to previous regimens/drugs
- To compare PFS/OS/response with outcome of last treatment before genomic profiling

Inclusion Criteria (selected)

This registry will include cancer patients for which broad genomic profiling is indicated, for example:
- Cancer with high mutational load and suspicion of regular or frequent formation of neoantigens
  - skin, lung, stomach, esophagus, colorectum, bladder, uterus, cervix, liver, head and neck, kidney, breast
  - lymphoma B-cell
- Any other neoplastic disease where molecular targeting is performed but treatment fails
- Cancer of unknown primary origin (CUP)
- Planned or already carried out comprehensive genomic testing as of Jan 1, 2016
- Signed written informed consent, age 18 years or over

Status (as of March 2019)

Site	Patients
UK Graz / Innere Medizin - Onkologie	197
PMU Salzburg / Innere Medizin III	115
UK Krems / Innere Medizin II	27
LKH Feldkirch / Innere Medizin II	12
Ordensklinikum Linz / Interne I	8
KH St. Vinzenz Zams / Innere Medizin	1
UK Innsbruck / Innere Medizin V	0
TOTAL	**360**

Note: This registry will not initially register patients who are tested for only 1-3 mutations by conventional means, but in patients undergoing genomic profiling. The results of such comprehensive test systems based on NGS will be compared with previously existing tests for mutations in single or very few genes.

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