Virtual Tumor Boards – challenges and opportunities

Christian Fegeler
IV Jornada de Oncología Médica, Puerto Varas, 23.08.2018
Paradigm shift to precision medicine

Past: symptom-based intuitive medicine

Today: modell-based evidence-based medicine

Tomorrow: algorithm-based precision medicine

Application of rules, algorithms and reference databases enable traceable clinical decision-making aids and precise and efficient care.

Source: vgl.: Wilkens 2016
The Scientific Challenge: molecular revolution in medicine is just beginning

Genomics
≈ 25,000 Gene

Transcriptomics
≈ 100,000 Transkripte

Proteomics
≈ 1,000,000 Proteine

Metabolomics
≈ 3,000 Metaboliten
data + context = information
The medical challenge:

Make globally distributed knowledge ...

... available for local patient care
Challenges and Opportunities

• Paradigm shift in knowledge management
• Digitalisation
• Data and information quality
• Individualisation ("n of 1 cohort")
• Big Data
Challenges to Opportunities

From individuality…

To Knowledge network

…and individualized therapy
Institute for Personalized Medicine

- founded in 2016
- Non-Profit-Organisation
- located in Heilbronn
- supported by Dieter Schwarz Foundation
- 12 own staff
- Applied science cluster and translation
Non-comparative, Open-label, Multiple Cohort, Phase 1/2 Study to Evaluate Nivolumab in Patients With Virus-associated Tumors (CheckMate 358): Efficacy and Safety in Merkel Cell Carcinoma

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VITU - Virtuelles Tumorboard
Melden Sie sich an, um an einer Konferenz teilzunehmen.
Mit MOLIT anmelden
... our molecular tumor board (MTB)

- started in May 2017
- weekly conference
- Multidisciplinary (Research + Clinic)
- supplements organ-specific tumor conferences as needed
Sustainable Response of a Patient With Metastasized Pancreatic Cancer and a Hypermutational Phenotype to Immunotherapy. New Therapeutic Concept for a Rare Subtype?

CASE REPORT

A 76-year-old woman was referred to our clinic with a suspicious lesion in liver segment VI after an abdominal ultrasound was performed in the routine setting. Besides occasional minor abdominal discomfort, the patient was asymptomatic. A biopsy specimen of the liver lesion revealed a poorly differentiated carcinoma, with tumor cells displaying a partly pleomorphic, signet ring or spindle cell appearance, fitting to the metastatic presentation of either a carcinoma of the bile duct or pancreatico-biliary system.

for whole-exome sequencing and sequenced on an Illumina HiSeq next-generation sequencing platform (Illumina, San Diego, CA) by CeGaT (Tuebingen, Germany). After bioinformatic filtering of germline variants and manual assertion of the called variants, a high tumor mutational burden (TMB) with 18 mutations/Mb was detected. The most relevant sonatic driver mutations were a loss-of-function stop mutation within FANCN (E472*) and an activating mutation in BRAF (V600E). No mutations in KRAS and genes involved in DNA mismatch repair
personalized immunotherapy leads to tumor regression
Workflow from tumor tissue to MTB report

1. Treatment case
   - Obtaining the tumor material of the patient (CT or sonographically controlled or surgical specimen)
   - Sample shipment
   - DNA sequencing (NGS)
   - Bioinformatics

2. Molecular diagnostics
   - Clinical evaluation
   - Validation

3. Molecular tumor board
   - MTB-treatment recommendations

Roles:
- Patient
- "Tissue team"
- Labor team
- Bioinformatician
- Clinical oncologists, human geneticists, biologists, study physicians
Virtual Tumor Board as an IT tool set

**Data collection and preparation**
- Report of molecular diagnostics
- Supplement to relevant data from the clinic
- Search for similar cases in the literature
- Search for available therapy options (studies)
- Validation
- MTB-treatment recommendations
- Review

**MTB conference**

**Follow-up individual case**

**Dynamic integration of information, queries as needed**

**Source independent search tool**

**Teleconference**

**Follow-up workflow**
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<tr>
<th>Erstelldatum</th>
<th>Fallnummer</th>
<th>Patient</th>
<th>Geburtsdatum</th>
<th>Diagnose</th>
<th>Status</th>
<th>Statusbeschreibung</th>
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Opportunity 1:
from
digital data
to
digital workflows

Data
• clinical data
• lifestyle
• molecular diagnostics

Analysis
• Connected data
• Machine learning
• Integration of knowledge

Integration of new knowledge

Patient individual model

Individual treatment
• Patient-doctor conversation
• Tumor board
• Expert involvement

personalized therapy

Patient Reported Outcome

MOL\textsuperscript{IT}
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MOLIT Framework an interoperable toolbox

- Platform for patient generated data
- Order Entry Communication
- Virtual Tumorboard (VITU)
- Knowledge Management Toolset
- Study Platform

MOLIT Framework

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Opportunity 2:

interoperability enables different usage contexts
Opportunity 3: interoperability enables cooperation

Example: www.cbiopoportal.org
### 33 Mutations (page 1 of 4)

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380 Copy Number Alterations (page 1 of 38)

source, 21.08.2018: http://www.cbioportal.org/patient?studyId=ucec_tcga_pub&caseId=TCGA-BK-A0CC
Source, 21.08.2018:
http://www.cbioportal.org/index.do?cancer_study_list=ucec_tcga_pub&cancer_study_id=ucec_tcga_pub&genetic_profile_idsPROFILE_MUTATION_EXTENDED=ucec_tcga_pub_mutations&Z_SCORE_THRESHOLD=2.0&RPPA_SCORE_THRESHOLD=2.0&data_priority=0&case_set_id=ucec_tcga_pub_sequenced&case_ids=&gene_set_choice=user-defined-list&gene_list=POLE%3A+MUT+%3D+P286+MUT+%3D+V411+MUT+%3D+L424+MUT+%3D+gene_set_selection=null&tab_index=tab_visualize&Action=Submit
Opportunity 4:

Case series are data with context
Classification of different study types

*1, sometimes known as experimental research; *2, analogous term: interventional; *3, analogous term: noninterventional or nonexperimental

This scheme is intended to classify the study types as clearly as possible. In the interests of clarity, we have excluded clinical epidemiology—a subject which borders on both clinical and epidemiological research (3). The study types in this area can be found under clinical research and epidemiology.
Draft characteristics of a good case series are:

- Clearly defined question.
- Well-described study population.
- Well-described intervention.
- Use of validated outcome measures.
- Appropriate statistical analyses.
- Well-described results.
- Discussion/conclusions supported by data.
- Funding source acknowledged.

Challenges and Opportunities

• Paradigm shift in knowledge management
• Digitalisation
• Data and information quality
• Individualisation ("n of 1 cohort")
• Big Data

• Digital workflows
• Interoperability
• Case series
Gracias