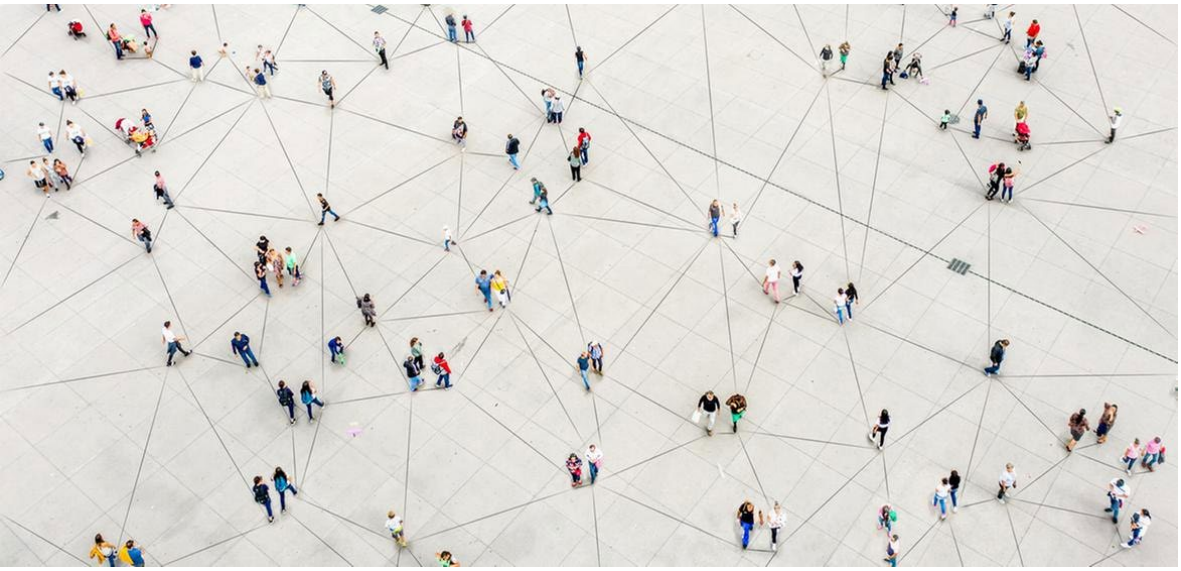
Oncological care

Bringing personalized tumor therapy to life: three recommendations

Two new publications by oncological associations in Germany investigate the prerequisites for efficient, comprehensive personalized tumor therapy.[1,2] This article explores their most important conclusions.



More networking and a functioning infrastructure

What is needed for the best possible care of oncology patients? The Bavarian State Parliament asked this question in a hearing on the Bavarian Cancer Registry in October 2020. In their statement, four specialist associations[a] involved in oncological care made it clear what is essential in terms of quality of treatment: to network all care participants, and to create the technical and organizational infrastructure necessary for this.[1]

The request for more networking can also be found in the new consensus paper of Deutsche Krebshilfe (German Cancer Aid, DKH). The DKH working group "Molecular Diagnostics and Therapy" defines the prerequisites for making comprehensive oncological treatment – based on personalized tumor therapy – a reality throughout Germany.[2]

The following overview summarizes the three key recommendations of the consensus paper, and shows initial examples of implementation.

1. Promote further training and closer collaboration

The consensus paper is primarily concerned with structural requirements:[2]

• Specific training courses for physicians, demonstrating the current possibilities and limits of molecular tumor diagnostics – so that they can be offered to suitable patients in a timely manner.

- Close cooperation between molecular pathologists and clinically practicing physicians – to ensure the availability of molecular tumor diagnostics.
- National harmonization of molecular genetic findings reports – to promote exchange between the various treatment centers.

2. Simplify access to personalized tumor therapy options

After a treatable aberration has been diagnosed, the patient often has insufficient access to targeted therapy options. As a solution, the authors of the consensus paper suggest concentrating personalized tumor therapy in specialized centers – for the following reasons:[2]

- This focus facilitates discussions with payers when it comes to reimbursing "off-label" drugs (see 3: Financing).
- The networked centers could offer patients with rare genetic mutations the option to participate in clinical studies.

ESMO[b] also recommends performing multigene sequencing in large centers so that these patients receive access to innovative therapy options – an approach which also supports clinical research.[3]

Examples of networked centers in Germany

In Germany, there are already initial partnerships between treatment centers, for example:

• The NCT DKTK MASTER program (Molecularly Aided Stratification for Tumor Eradication) of the Nationales Centrum für Tumorerkrankungen (National Center for Tumor Diseases, NCT) Heidelberg and the Deutsches Konsortium für Translationale Krebsforschung (German Consortium for Translational Cancer Research, DKTK) offers overall genome sequencing with personalized therapy recommendations at all sites for young patients or patients with rare tumors.[4,5]

• The national network of genomic medicine (nNGM [nationales Netzwerk Genomische Medizin]) with over 15 clinics treats patients with lung tumors with its range of molecular diagnostics and treatment options.[6]

• Oncology centers in Baden-Württemberg have joined forces in the "Competence Network for Personalized Oncology Baden-Württemberg". The network aims to advance innovative study activities and is aimed at patients with advanced tumor diseases with its diagnostic and treatment options.[7]

• With its "Network of Oncological Top Centers", DKH is also committed to ensuring that comparable care structures are created, for example in central municipal hospitals.[8]

3. Secure financing for personalized therapy approaches

The consensus paper of the DKH also sees the specialized treatment centers as an important prerequisite for establishing financing models with health insurance companies. With their structured treatment processes, the centers can offer the high quality, transparency, and cost efficiency demanded by payers.[2]

Baden-Württemberg is considered a successful example of financing with the "Centers for Personalized Medicine (Zentren für Personalisierte Medizin, ZPM)". Among other things, they have committed themselves to specific quality standards and treatment processes – in particular for molecular tumor boards.[9,10]

So far, the comprehensive financing of companion diagnostics in the inpatient sector is still unresolved; only individual centers have OSMC[c] contracts.[11,12] In addition, the German Society of Pathology published a position paper with concrete proposals in September 2020 – including reimbursement via NETM[d] applications and a cost allocation in the case lump-sum system.[12]

The common language: A uniform classification system is required

A common understanding regarding the clinical evaluation of genetic changes is decisive for the desired cooperation between treatment centers.[3] At present, three validated classification systems are in use. A standardization based on the model of human genetics would simplify interdisciplinary exchange.[13]

A brief overview of the classification systems:

USA: ACMG/AMP/ASCO/CAP[e]

The US scoring system orders somatic genetic variants according to 4 stages (tiers):[14]

I. With strong clinical significance
II. With potential clinical significance
III. With unknown clinical significance
IV. Benign or probably benign

For this purpose, the system uses evidence information from population and sequence databases, among other information, and employs prediction algorithms.[14]

EUROPE: ESCAT[f]

The classification system of ESMO divides the genetic target structures (targets) into 6 levels (tiers) on the basis of clinical evidence according to their significance for patient management:[15]

I. Targets for routine use in clinical decisions.
II. Targets that are likely to define a patient population that benefits from targeted therapy, but for which additional data is required.
III. A clinical benefit was previously demonstrated in other tumor types or for similar molecular targets.
IV. Preclinical evidence of treatability.
V. There is evidence that the target supports a co-targeting approach.
VI. No evidence of treatability.

Germany: NCT/DKTK MASTER

The Heidelberg classification system divides genetic changes into 4 evidence levels (with subclasses) according to the association between a molecular change and the response to a pharmaceutical active ingredient: Levels 1 and 2 according to clinical evidence, levels 3 and 4 according to preclinical evidence. The total of 7 categories range from 1A (approved medicinal product) to 4 (biological rationale available without preclinical or clinical data on the efficacy of the substance).[4,16]

Possible solution approach: harmonization with open-access meta-databases

One way to harmonize these classification systems would be in freely accessible (open-access) meta-databases, such as search.cancervariants.org. In this case, 6 knowledge databases were merged, comprising close to 13,000 interpretations. The expansion of knowledge improved the interpretation rate with regard to a potential clinical relevance of genetic changes: from 33% per individual database to 57% with this meta-database.[17] This demonstrates how establishing common standards and fostering a culture of "data sharing" can enable the comprehensive use of personalized tumor therapy.[18]

Abbreviations

a Deutsche Krebsgesellschaft (German Cancer Society, DKG), Deutsche Gesellschaft für Senologie (German Society for Senology, DGS), Deutsche Gesellschaft für Pathologie (German Society for Pathology, DGP) and Deutsche Gesellschaft für Gynäkologie und Geburtshilfe (German Society for Gynecology and Obstetrics, DGGG)

b ESMO: European Society for Medical Oncology

c OSMC: Outpatient specialist medical care

d NETM: New examination and treatment method

e ACMG/AMP/ASCO/CAP: American College of Medical Genetics and Genomics (ACMG) Association for Molecular Pathology (AMP) American Society of Clinical Oncology (ASCO), College of American Pathologists (CAP)

f ESCAT: ESMO Scale for Clinical Actionability of Molecular Targets

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