CCBIO Opinion

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PROMISES AND PROBLEMS OF PRECISION ONCOLOGY

Since 1999, when the foundation document for precision medicine was published[1], the term precision oncology has been used to substantiate the importance of genomic information for risk assessment, diagnosis, and treatment selection in cancer.

Increasingly more genomic tests are being conducted in clinical practice. As early as 1998, the BCR-ABL rearrangement in chronic myeloid leukemia was shown to be successfully targeted with imatinib. In 2012, an anti-tumor activity of the poly (adenosine diphosphate [ADP]–ribose) polymerase (PARP) inhibitor in patients with ovarian cancer with BRCA1/BRCA2 mutations was shown. Additionally, over the years, non-small cell lung cancer has emerged as an architype for genomic data use for optimal treatment selection throughout the treatment course. The introduction of genomic testing is both resource intensive and expensive, and as usage increases, a multidisciplinary decision-making approach is required. The introduction of more and more targeted drugs on the market will further increase the complexity.

The concept of precision oncology was introduced with the hope that it could radically change patient management. However, more than two decades after its introduction, the approach has not, with a few exceptions, lived up to expectations. Hopefully, the different ongoing drug rediscovery initiatives that redefine approved drug use beyond their labels to patients with potentially actionable variants, will represent a move forward.

Due to decades of scientific work and technical innovation, the molecular understanding of tumor biology has advanced. Clearly, the prospects of precision oncology depend not only on genomic data in a static map but also on biological real-time understanding of spatial resolution and interrogation of cell–cell interactions to deliver the right treatment to the right patient at the right dose and at the right time. Spatial omics and multiplexed imaging are needed to explore cancer subclones and/or molecular biomarkers within their native spatial contexts. Technologies that allow the integration of multi-omics data are being developed. Once in place, the full potential of molecular profiling and precision oncology will be evident. Interestingly, all approaches used today to determine treatment response are based on tumor load and do not generate functional parameters about therapy effects. Notably, the use of single-cell signaling profiling and machine learning approaches to identify predictors for 5-year overall survival 24 hours after the first chemotherapy cycle in acute myeloid leukemia patients was recently demonstrated[2]. Functional diagnostics providing "next generation biomarkers" are necessary to generate this real-time information and algorithms to discriminate between therapy responders and non-responders, allowing early therapy adjustments in models for adaptive and precise treatment. ••

References

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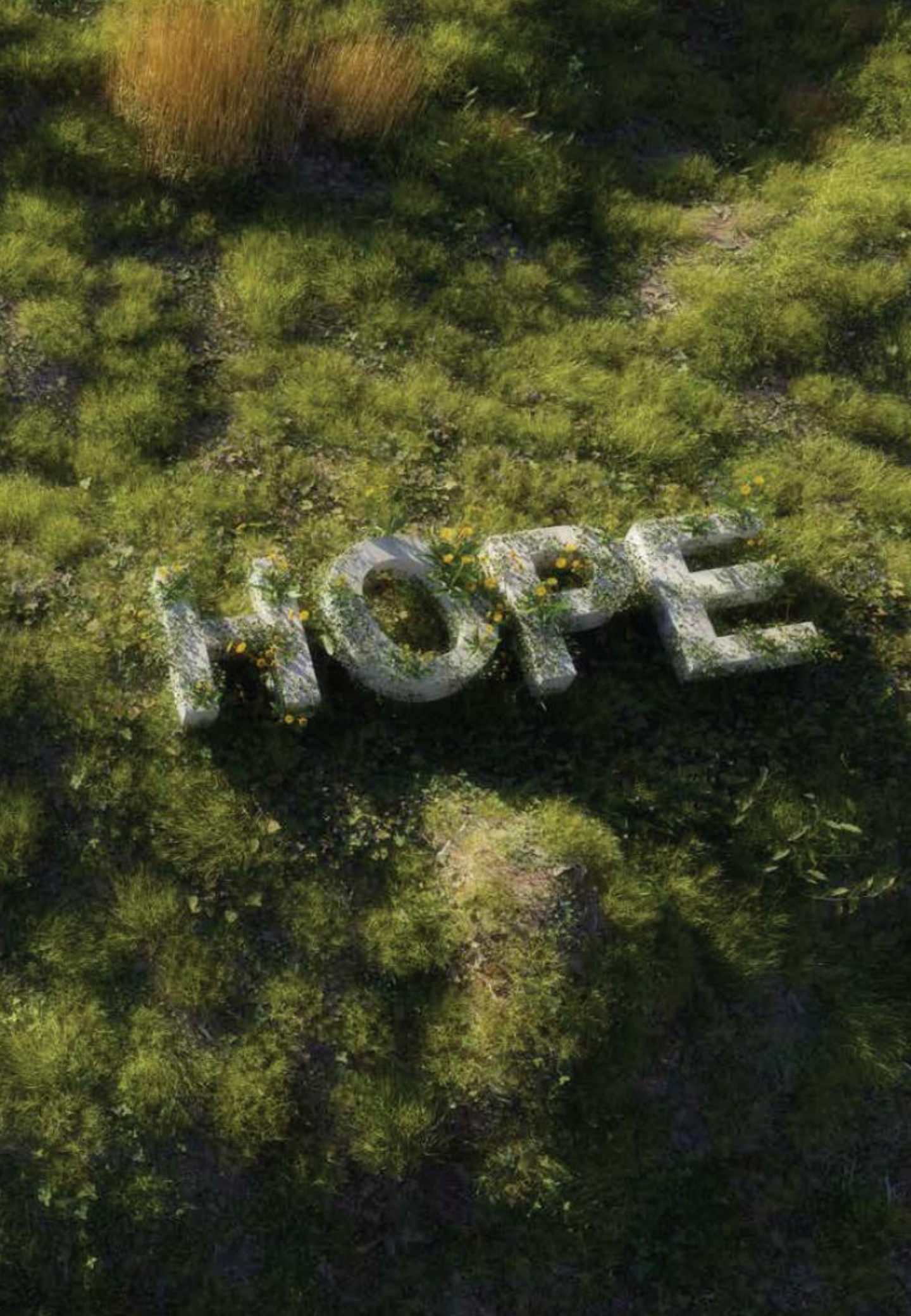
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