Dynamic precision medicine: a new paradigm for minimal residual disease

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Abstract

Background: Current precision medicine (CPM) matches patients to therapies using traditional biomarkers, but inevitably resistance develops. Dynamic precision medicine (DPM) is a new evolutionary guided precision medicine (EGPM) approach undergoing translational development. It tracks intratumoral genetic heterogeneity and evolutionary dynamics, adapts as frequently as every six weeks, plans proactively for future resistance development, and incorporates multiple therapeutic agents. Simulations indicated DPM can substantially improve long-term survival and cure rates in a cohort of 3 million virtual patients representing a variety of clinical scenarios. Given the cost and invasiveness of monitoring subclones frequently, we sought to determine the value of a short DPM window of only two 6-week adaptations (“moves”). Objective: develop an evolutionary classifier to identify patients who will benefit from DPM, and define the required duration of intensive subclonal monitoring. Methods: In a new simulation, nearly 3 million virtual patients, differing in DPM input parameters of initial subclone compositions, drug sensitivities, and growth and mutational kinetics, were simulated as previously described. Each virtual patient was treated with CPM, DPM, and DPM for two moves followed by CPM. Results: The first two DPM moves provide similar average benefit to a five-year, 40-move sequence in the full virtual population. If the first two moves are identical for DPM and CPM, patients are less likely to benefit from DPM (65% negative predictive value). A patient subset (20%) in which 2-move and 40-move DPM provide closely similar outcomes has extraordinary predicted benefit (Hazard ratio (HR)-DPM/CPM 0.03). Conclusion: The first two DPM moves provide most of the clinical benefit of DPM, reducing the duration required for intensive subclone monitoring. This also leads to a novel multicomponent evolutionary classifier selecting patients who will benefit: those in whom DPM and CPM recommendations differ early. These advances bring DPM (and potentially other EGPM approaches) closer to potential clinical testing.

Do you have any conflicts of interest?

Yes, I have a conflict of interest.

Chief Scientific Officer (uncompensated) of Onco-Mind, LLC that owns relevant patents