Real-world study to evaluate the clinical performance of a computational method in precision oncology.

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Background:

In recent years, precision medicine has increasingly been integrated into routine clinical oncology care. However, interpretation of large amounts of biological information can be challenging in daily clinical practice settings. We previously demonstrated that digital drug assignment (DDA), an artificial intelligence-based computational method that ranks associated targeted therapies based on the totality of available genomic data rather than matching one drug to one biomarker, was predictive of relative benefit of the agents as used in the SHIVA01 trial (Petak et al., 2021, doi: 10.1038/s41698-021-00191-2). Here, we collected real-world clinical outcome data from patients with solid tumors who received decision support where DDA was integrated to aid a molecular tumor board (MTB) and investigated the effectiveness of recommended therapies.

Methods:

Between 2016 and 2021, 208 patients with solid tumors were involved in our precision oncology program (69% gastrointestinal, 14% gynecological, 9% breast, 8% other tumors). In most cases targeted panel sequencing was carried out (50-gene panel: 51%, 591-gene panel: 45%).

Classification of the detected alterations and therapeutic ranking was performed by the DDA software tool as previously described. The output was assessed by the MTB that provided a strategy to the clinicians who made the final therapy decisions. DDA output scores were supportive for all molecularly targeted agents (MTAs) administered. Treatment lines after decision support with MTAs were compared with lines of standard agents (STs) retrospectively and evaluated by best overall response, log-rank test of progression-free survival (PFS), and durable clinical benefit (DCB).

Results:

Of all 208 patients, 81 were treated with MTAs and 59 with STs after DDA, implying 114 and 97 therapeutic lines, respectively. Disease control rate (DCR) of the suggested MTAs was 40% (0 CR, 9 PR, 37 SD, 43 PD, 25 lost to follow-up), while DCR for STs was 25% (1 CR, 3 PR, 20 SD, 48 PD, 25 lost) ($p=0.025$). PFS value was available for 88 MTA and 71 ST lines. Log-rank test revealed a significantly longer median PFS for MTAs than STs: 4 vs. 2.5 months, respectively ($p<0.001$). Proportion of patients who reached DCB of 6 months was 32% in the MTA and 11% in the ST group ($p<0.001$). DCB at 9 months was 19% and 5% in the MTA and ST cohorts, respectively ($p=0.003$).

Conclusions:

This study revealed clear clinical benefit for targeted therapies over conventional treatments used in daily practice, where MTB was aided by a computational tool to interpret complex molecular data. After the previous clinical validation, here we show that integration of DDA into real-world clinical setting is feasible and safe. The results fit well into the trend of targeted therapies becoming a routine procedure and underscore the importance of precision oncology decision support by advanced computational tools.