早期臨床試験であっても個別化治療は治療成績を改善する(Abstract 11520)

第I相試験において適切な治療が患者の予後を改善する

Precision medicine yields better outcomes for patients in phase I clinical trials

13,000人超の患者を組み入れた346の第I相臨床試験のメタ解析の結果、腫瘍の分子学的特性に基づいた治療を選択された患者は、有意に予後が良好であることが示された。適切な治療を用いた群では腫瘍縮小率が30.6%であり、適切な治療を用いてない群では4.9%であった。無増悪生存期間においても、適切な治療群で長かった(期間中央値5.7か月対2.95か月)。筆者らは、第I相試験の患者選択においても腫瘍バイオマーカーはますます用いられるべきである、と述べている。このスタディ結果は、2016年American Society of Clinical Oncology年次集会で発表された。

Full Text

A meta-analysis of 346 phase I clinical trials involving more than 13,000 patients found that patients whose treatment was selected based on the molecular characteristics of their tumor had significantly better outcomes. The study was presented at the 2016 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago.

"Our study suggests that, with a precision medicine approach, we can use a patient's individual tumor biomarkers to determine whether they are likely to benefit from a particular therapy, even when that therapy is at the earliest stage of clinical development," said lead study author Maria Schwaederle, PharmD, of the Center for Personalized Cancer Therapy, University of California-San Diego School of Medicine. "This strategy often results in good outcomes for patients, and I hope it will encourage and reassure doctors and patients considering enrollment in precision medicine-based phase I trials."

Previous meta-analyses of phase II and phase III trials by the same researchers observed similarly improved outcomes with precision medicine approaches.

According to the authors, this is the first study to show that such benefits are apparent even at the first stage of clinical development. It suggests that tumor biomarkers should be increasingly used to select patients for phase I clinical trials.
The study examined efficacy and safety data from 346 phase I trials published between 2011 and 2013. The analysis included 58 treatment arms that employed precision medicine – defined as using biomarkers to select patients for treatment – and 293 that did not (all but one of these precision medicine trials evaluated a targeted agent: the trial evaluated the chemotherapy drug topotecan, which is believed to inhibit hypoxia-inducible factor 1-alpha (HIF-1 alpha), and patients in that trial were tested for this marker).

The researchers found that in treatment arms employing precision medicine, tumor shrinkage rates were 30.6%, compared to 4.9% in those that did not. Patients in precision medicine arms also had a longer progression-free survival compared to other arms (median 5.7 months vs. 2.95 months).

Results were similar in a sub-analysis that included 57 trials of targeted therapies – drugs that target specific genes or proteins found in cancer cells. In this group, treatment arms using biomarkers to assign patients to treatments had tumor shrinkage rates of 31.1%, compared to 5.1% for those that did not. Additionally, researchers found that matching patients to therapy based on genomic (DNA) biomarkers resulted in higher tumor shrinkage rates (42%) compared to protein biomarkers (22.4%).

In this analysis, the high tumor shrinkage rates and prolonged time to disease progression observed with precision medicine approaches suggest that phase I studies, which have traditionally focused on safety, can also provide important insights into efficacy and the patients likely to benefit most. Incorporating survival endpoints into phase I trials may help accelerate development of important new therapies, the authors suggested.

"Precision medicine is not the future of cancer care, it is the present. This study reinforces that the more we personalize treatment to the patient and the tumor, the better the outcomes – even in the earliest phases of research," said Don S. Dizon, MD, FACP, ASCO spokesperson. "This is the same approach ASCO's TAPUR trial is using, and we anticipate it will also bring new insights that lead to better therapies for patients in need."

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