個別化医療によりがんの治療選択肢が広がる可能性がある（Abstract LBA11511）

個別化医療により進行がん患者の治療選択肢が広がる可能性がある

Precision medicine approach may expand therapeutic options for patients with advanced cancers

腫瘍内分子異常を有する患者と対応する分子標的治療とを適合させた、第II相試験の有望な早期結果が報告された。12の異なる型の進行がんを有する患者129人中29人において、FDAが承認した適応以外の薬剤が奏効した。特定の分子変異を有する4つの腫瘍タイプにおいて、有望な奏効性が認められたことから、これらの腫瘍を有する他の参加者にも薬剤の使用が拡大されている。有効性が最も確実視されたのは、HER2異常を有する患者であった。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

Researchers reported encouraging early results from a phase II trial that matches patients with molecular abnormalities in the tumor to corresponding targeted treatments. Twenty-nine of 129 patients with 12 different types of advanced cancers responded to drugs outside of U.S. FDA-approved indications. The promising responses seen in four tumor types with specific molecular alterations has already led to expansion of these tumor cohorts to additional participants.

The study was presented at the 2016 American Society of Clinical Oncology (ASCO) Annual Meeting.

"With genomic testing of tumors becoming increasingly available, studies such as ours will help more patients benefit from precision medicine approaches," said lead study author John D. Hainsworth, MD, senior investigator at Sarah Cannon Research Institute in Nashville, TN. "Although it is still early to draw conclusions, our findings suggest that, for example, HER2-targeted therapy could be expanded beyond the current indications of HER2-positive breast and gastric cancers. Our study gives strong early signals for activity of HER2-targeted therapy in HER2-amplified colorectal cancers (those with extra copies of *HER2* gene), and possibly other HER2-positive cancers."

MyPathway is an ongoing non-randomized, open-label trial that evaluates four treatment regimens in patients with advanced cancer for whom no beneficial treatment is available. This is a nationwide study with 39 currently participating sites.

To be eligible for the study, patients must have had previous molecular studies of the cancer showing abnormalities in the HER2, BRAF, Hedgehog or EGFR pathways. Patients were then matched with drugs targeting those abnormalities. Patients received a combination of trastuzumab and pertuzumab if they had HER2 abnormalities (amplification, overexpression, or mutation); vemurafenib for BRAF mutations; vismodegib for Hedgehog pathway mutations; and erlotinib for EGFR mutations. Only tumor types outside of current indications for these treatments were eligible.

Among the first 129 patients enrolled in the study, 82 had alterations in HER2, 33 in BRAF, 8 in Hedgehog and 6 in EGFR. All patients had an advanced solid tumor and had received a mean of three prior therapies. A total of 29 patients with 12 different types of cancer responded to targeted treatment. Fourteen responders have progressed after a median of 6 months of treatment (range 3-14 months); 15 responses are ongoing at 3+ to 11+ months.

The most promising efficacy was seen among patients with HER2 abnormalities – 7 of 20 patients with colorectal cancer, 3 of 8 with bladder cancer, and 3 of 6 with biliary cancer experienced objective responses (tumor shrinkage of 30% or more). Based on these results, recruitment to each of these groups has been expanded.
The group of patients with lung cancer and BRAF mutations will also be expanded. Among the first 15 patients in that group, 3 had objective responses and 2 had stable disease lasting for at least 4 months.

"This study speaks to the incredible potential of precision medicine to help us identify new treatments, but it also underscores the need to explore this genomic-based testing and treatment approach in a learning environment, like a clinical trial," said Sumanta Kumar Pal, MD, ASCO expert in developmental therapeutics. "It's likely there are factors that we are not yet aware of that explain why certain patients benefit from targeted therapies while others don't, even when their tumors have the same abnormality. We need to find these answers so we can match more patients to potentially beneficial treatments and spare patients from treatment that is unlikely to improve or prolong their lives."

The study is designed to accrue up to 500 patients. Groups that show low benefit will be stopped early, while groups that demonstrated efficacy will be expanded. The researchers also plan to incorporate emerging new regimens targeting these pathways. For example, cobemetinib, a MEK inhibitor, will soon be added to vemurafenib for patients with BRAF mutations. Incorporation of new agents targeting additional molecular abnormalities is also planned in the future.

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