

## ステージ4のがん患者においては併用療法が有益な可能性がある

低用量のIL-2および13-cisレチノイン酸投与を受けた進行がん患者は生存率が改善する  
Improved survival for patients with advanced cancers who received lower doses of IL-2 and 13-cis retinoic acid

インターロイキン2および13-cisレチノイン酸による維持療法は、様々なステージ4のがん患者における生存率を上昇させる安価な方法となり得る、との研究結果が2012年AACR学会で発表された。ある転移性メラノーマ患者が通常の18M UI/m<sup>2</sup>の高用量インターロイキン2 (IL-2) に忍容性がなく、しかし低用量が奏効した後の1995年に、研究者らは進行がん患者における維持療法の評価を開始した。このスタディにおいては、腫瘍の種類は様々であるが全員ステージ4の患者500人を評価した。通常のがん治療後に、患者は週5日のIL-2 (1.8×106IU) 自己皮下注射および経口RA (0.5mg/kg) 投与を、3週間のサイクルで連続2サイクル行いその後1週間休薬する治療を1年間施行された。追跡期間中央値60か月後には、ナチュラルキラー細胞 (NK細胞) 数が増加し血管内皮増殖因子が減少していた。15年無病生存期間および全生存率はそれぞれ、32.6%および36.8%であった。卵巣がん、非小細胞肺癌、肉腫の心臓転移、大腸、胃、腎細胞がん、メラノーマ、頭頸部がん、乳、膵および再発性卵巣がんを含む全てのがんにおいて有益であった。

### Full Text

Maintenance therapy with interleukin-2 and 13-cis retinoic acid may be an inexpensive method for increasing survival in patients with a variety of stage 4 cancers, according to data reported at the AACR Annual Meeting 2012.

Francesco Recchia, M.D., director of oncology at the Civilian Hospital in Avezzano, Italy, started evaluating the maintenance therapy in patients with advanced disease in 1995 after one patient with metastatic melanoma did not tolerate the usual 18 M UI/m<sup>2</sup> high-dose interleukin-2 (IL-2) therapy.

"The patient was treated with lower doses, and he had a wonderful, long-lasting response," he said.

After this observation, Recchia conducted several other studies of IL-2 with or without retinoic acid (RA). "I was encouraged by these preliminary results, and therefore, I conducted a phase II study of this drug combination in 80 patients who had obtained a clinical benefit from chemotherapy. The results were very interesting."

The researchers evaluated 500 patients with different tumor types, but all with stage 4 disease. After their normal cancer treatment, patients were assigned to self-administered subcutaneous IL-2 (1.8×106 IU) and oral RA (0.5 mg/kg) five days a week for two consecutive cycles of three weeks, followed by a one-week rest, for one year. After a median follow-up of 60 months, researchers reported increased numbers of natural killer cells (NK cells) and a decrease of vascular endothelial growth factor. The 15-year disease-free survival and overall survival rates were 32.6 percent and 36.8 percent, respectively.

"These studies had such good and unexpected results that I thought it would not be ethical to conduct a randomized study without this immunotherapy regimen," Recchia said. "All types of cancer treated had a benefit from this immunotherapy regimen: ovarian cancer, non-small cell lung cancer, cardiac metastases of sarcoma, colorectal cancer, gastric cancer, renal cell carcinoma, melanoma, head and neck cancer, breast cancer, pancreatic cancer and recurrent ovarian cancer."

Despite the limitations of different cancer populations, the researchers reported a marked improvement in the five-year overall survival rate for the most commonly treated metastatic cancers compared with National Cancer Institute Surveillance Epidemiology and End Results data: breast (42.7 percent vs. 23.3 percent), lung (26.4 percent vs. 3.6 percent), colorectal (43.6 percent vs. 11.7 percent) and renal (23 percent vs. 11 percent).

Immunotherapy with IL-2 has fallen out of favor in place of newer monoclonal antibodies, according to Recchia. Although his results appear promising, a blinded, controlled, randomized trial would be needed before clinicians could begin using this maintenance regimen.

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