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Immunotherapy as strategy to maintain response from chemotherapy in stage IV cancer

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Background: Even if patients with stage IV cancer (AC) may have prolonged remissions with chemotherapy (CT), the majority of them, will eventually relapse. In vitro studies suggest that natural killer (NK) cells mediate lytic activity against cancer cell lines and that high expression of vascular endothelial growth factor (VEGF) promotes tumor progression through neoangiogenesis. We have shown that low-dose interleukin-2 (IL-2) and 13-cis retinoic acid (RA) increased NK cells and decreased VEGF, in patients with AC and a clinical benefit on CT (Clin Cancer Res 7:1251, 2001). We hypothesized that IL-2 and RA, increasing NK and decreasing VEGF, could improve disease-free survival (DFS) and overall survival (OS) in a minimal residual disease setting. Primary endpoint was the evaluation of NK cells and VEGF; secondary endpoints were DFS, OS and toxicity.

Methods: 500 patients with stage IV cancer, who had had a clinical benefit from CT, were given immunotherapy to maintain response to CT. Immunotherapy consisted of subcutaneous IL-2, 1.8×106 IU and oral RA, 0.5 mg/Kg for 5 days/week, 3 weeks/month, until progression. NK cells, VEGF, response and toxicity were assessed every 4 months.

Results: After a median follow-up of 112 months (range 63-200), a total of 4400 courses of chemotherapy and 2634 courses of immunotherapy were delivered. A statistically significant improvement of NK cells [from a mean of 309 ± 76/mm3 to a mean of 579 ± 74/mm3 ($p < 0.001$)] and a decrease of VEGF [from a mean of 520 ± 75 pg/mm3 to a mean of 150 ± 12 pg/mm3, ($p < 0.001$)], were observed. 18-years DFS and OS were 29% and 32%, respectively. A significant improvement, with respect to NCI SEER data (*), was observed in the 5-year OS rate for the most common treated AC: Breast cancer 55% vs. 6% *; Lung cancer 22% vs. 4.3% *; Colorectal cancer 43.5% vs. 21%*. No WHO grade 3 or 4 toxicity was observed, while grade 2 cutaneous toxicity and fever occurred in 20% and 13% of patients, respectively.

Conclusions: Our data show that immunotherapy with IL-2/RA, may determine, with an acceptable toxicity profile, a statistically significant improvement of NK cells, a decrease of VEGF, and better 5-year survival rates with respect to NCI SEER data, for all major cancers.

Biography

Francesco Recchia MD has completed his M.D at the age of 24 years from RomeUniversity and postdoctoral studies from University of Texas, MD Anderson Hospital.He is the director of Medical Oncology at The Civilian Hospital Avezzano, affiliated withthe University pf Lï¿½Aquila, Italy. He has published 247 papers in reputed journals and heis serving as an editorial board member in several Oncology journals.

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