Lymphocytes prognostic in breast cancer

The density of stromal tumour-infiltrating lymphocytes is a possible prognostic factor for women with triple-negative breast cancer, according to a study based on data from two randomised phase 3 trials using contemporary adjuvant chemotherapy.

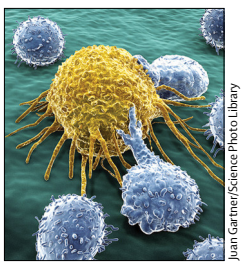
Lymphocytic infiltration in primary breast cancers was described decades ago, often in the context of medullary breast cancers, and some findings suggested prognostic value. "We wanted to prospectively validate these findings in triple-negative breast cancer...adjuvant trials", explains lead author Sylvia Adams (University Cancer Institute, New York, NY, USA). Her study assessed tumours for density of tumour-infiltrating lymphocytes from both intraepithelial and stromal compartments. With disease-free survival as the primary endpoint, association with tumour-infiltrating lymphocyte scores was determined by fitting proportional hazards models stratified on study.

386 (80%) of the 481 tumours assessed contained stromal tumour-infiltrating lymphocytes, and for every 10% increase in stromal compartments, there was a 14% reduction of risk of recurrence or death (p=0·02), an 18% reduction of risk of distant recurrence (p=0·04), and a 19% reduction of risk of death (p=0·01). 70 (15%) of tumours had intraepithelial tumour-infiltrating lymphocytes, but they were not significantly associated with patient outcomes.

"The issue now is how we incorporate this knowledge into improved outcomes for patients with triple-negative breast cancer", says Sherene Loi (Peter MacCallum Cancer Centre, Melbourne, Australia). "Why can some triple-negative breast cancer patients generate an anti-tumour immune response, whilst others cannot? Will T-cell checkpoint inhibition be effective given that these pathways are induced as a result of immune activation?" Loi continues, "There are ongoing efforts to provide guidance on the evaluation method, though at present, clinical utility of such a measurement, outside clinical trial settings, has not been established."

The authors propose that data for tumour-infiltrating lymphocytes should be prospectively collected in clinical trials. The next step is to implement these findings effectively into a practical, clinical cancer setting. "By therapeutically targeting and harnessing the immune system, we have a tremendous opportunity to improve cure rates in patients with triple-negative breast cancer," concludes Adams.

Alexandra Sklan



Juan Gartner/Science Photo Library

Lancet Oncol 2014

Published Online
August 8, 2014
http://dx.doi.org/10.1016/S1470-2045(14)70369-9

For the **study by Adams and colleagues** see *J Clin Oncol* 2014; published online July 28. DOI:10.1200/JCO.2013.55.0491

Adapted paediatric regimen benefits adults with ALL

A regimen adapted from an intensive paediatric regimen for treating acute lymphoblastic leukaemia (ALL) has been found to improve overall survival in adults with the disease.

During the past 20 years, development of risk-stratified, multi-agent, multi-phase treatment regimens for paediatric patients with ALL has resulted in proportions of patients greater than 95% acheiving complete remission, and 5-year event-free survival greater than 80%. However, therapeutic regimens for adults with ALL have been less effective, achieving overall survival of less than 50%.

Wendy Stock (University of Chicago Medicine, Chicago, IL, USA) said that many equally important reasons exist for the different outcomes in paediatric and adult patients with ALL. "In addition to differences in the actual treatment (drug dose, schedule), other potential explanations include that the biology of the disease changes as we age", she commented.

Within the past decade, studies have shown that older adolescents and young adults (aged 16–21 years) treated with paediatric ALL regimens achieved improved outcomes. In a recent multicentre phase 2 trial (NCT00136435), 92 patients aged 18–50 years with newly diagnosed ALL received treatment based on the Dana-Farber Cancer Institute Pediatric ALL Consortium regimen. 78 (85%) of the 92 participants achieved complete remission after 4 weeks of the induction phase of therapy; the 4-year disease-free survival for these patients was 69% (95% CI 56–78). For all 92 participants, the 4-year overall survival was 67% (95% CI 56–76).

Lead author Daniel DeAngelo (Dana-Farber Cancer Institute, Boston, MA, USA) said "Young children tolerate intensive therapy better than adults, who have more toxicities than pediatric patients. In this study, pancreatitis, thrombosis, liver toxicity rates were similar to those of older adolescents, and were tolerable in this adult population. Our data support the adoption of paediatric-inspired regimens for young adults. The question that needs to be answered is: what is the upper age limit for which one should consider the use of paediatric regimens? I argue that at least everyone under 30 should be treated based on a paediatric or a paediatric-inspired regimen."

Stock commented on this trial, "This is a wonderful stride forward in adult ALL. The Dana-Farber Consortium could deliver the paediatric–type regimen to an adult population up to age 50, and results are significantly better than historical controls."

Judith A Gilbert

Lancet Oncol 2014

Published Online
August 8, 2014
http://dx.doi.org/10.1016/S1470-2045(14)70382-1

For the **study by DeAngelo and colleagues** see *Leukemia* 2014; published online July 31. DOI:10.1038/leu.2014.229