Prospective validation of a 21-gene expression assay in breast cancer

Authors conducted a prospective trial in women with hormone-receptor–positive, human epidermal growth factor receptor type 2 (HER2)–negative, axillary node–negative breast cancer with tumors of 1.1 - 5.0 cm in the greatest dimension (or 0.6 to 1.0 cm in the greatest dimension and intermediate or high tumor grade) who met established guidelines for the consideration of adjuvant chemotherapy on the basis of clinicopathologic features. A reverse-transcriptase–polymerase-chain-reaction assay of 21 genes was performed on the paraffin-embedded tumor tissue, and the results were used to calculate a score indicating the risk of breast-cancer recurrence; patients were assigned to receive endocrine therapy without chemotherapy if they had a recurrence score of 0 to 10, indicating a very low risk of recurrence (on a scale of 0 to 100, with higher scores indicating a greater risk of recurrence).

Of the 10,253 eligible women enrolled, 1626 women (15.9%) who had a recurrence score of 0 to 10 were assigned to receive endocrine therapy alone without chemotherapy. At 5 years, in this patient population, the rate of invasive disease–free survival was 93.8%, the rate of freedom from recurrence of breast cancer at a distant site was 99.3%, the rate of freedom from recurrence of breast cancer at a distant or local–regional site was 98.7% , and the rate of overall survival was 98.0%.

Comments

This study has shown the practical application of gene expression profiling both in prognosticating breast cancers as well as selecting patients for endocrine therapy alone, thus avoiding the side effects of chemotherapy in low risk patients. It is hoped that a better understanding of gene expression in other cancers will help predict their biological behavior as well and help to tailor therapy accordingly.

Sparano JA, Gray RJ, Makower DF, Pritchard KI, Albain KS, Hayes DF, Geyer CE Jr, Dees EC, Perez EA, Olson JA Jr, Zujewski J, Lively T, Badve SS, Saphner TJ, Wagner LI, Whelan TJ, Ellis MJ, Paik S, Wood WC, Ravdin P, Keane MM, Gomez Moreno HL, Reddy PS, Goggins TF, Mayer IA, Brufsky AM, Toppmeyer DL, Kaklamani VG, Atkins JN, Berenberg JL, Sledge GW. Prospective validation of a 21-gene expression assay in breast cancer. N Engl J Med 2015;373:2005-2014.

Intravenous augmentation treatment and lung density in severe á1 antitrypsin deficiency (RAPID): a randomised, double-blind, placebo-controlled trial

Under the RAPID study, authors recruited eligible non-smokers (aged 18–65 years) in 28 international study centres in 13 countries if they had severe á1 antitrypsin deficiency (serum concentration <11 ìM) with a forced expiratory volume in 1 s of 35–70% (predicted). Patients where randomly assigned to receive á1 antitrypsin (A1PI) intravenously 60 mg/kg per week (n=93) or placebo (n=87) for 24 months.

The annual rate of lung density loss at total lung capacity (i.e at full inflation) alone was significantly less in patients in the A1PI group (1·45 g/L per year [SE 0·23]) than in the placebo group (2·19 g/L per year [0·25]; difference 0·74 g/L per year, p=0·03). However no differences between the groups were observed for the annual rate of lung density loss at functional residual volume (i.e at the end of a normal expiration). Treatment-emergent adverse events were similar between groups. One

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http://svimstpt.ap.nic.in/jcsr/Oct-dec15_files/js15.pdf

treatment-emergent adverse event leading to withdrawal from the study occurred in one patient (1%) in the A1PI group and ten occurred in four patients (5%) in the placebo group. One death occurred in the A1PI group (respiratory failure) and three occurred in the placebo group (sepsis, pneumonia, and metastatic breast cancer).

Comment

Severe á1 antitrypsin deficiency is a devastating condition associated with the development of emphysema in the thirties or forties of age, even in the absence of smoking. Previous studies on alpha1 antitrypsin supplementation in patients with deficiency of this enzyme had only assessed spirometry. These studies were unable to demonstrate any effect of enzyme supplementation on progress of emphysema. The present study used serial CT based lung density measurements, which is much more sensitive than spirometry and it demonstrated a reduction in the rate of progression of emphysema in the group supplemented with á1 antitrypsin than the placebo group. This is an additional example of successful treatment of an inherited enzyme deficiency through enzyme replacement.

Chapman KR, Burdon JG, Piitulainen E, Sandhaus RA, Seersholm N, Stocks JM, Stoel BC, Huang L, Yao Z, Edelman JM, McElvaney NG; RAPID Trial Study Group.. Intravenous augmentation treatment and lung density in severe á1antitrypsin deficiency (RAPID): a randomised, double-blind, placebo-controlled trial. Lancet 2015;386:360–8.

Comparative study of effectiveness and resistance profile of chloroquine and sulfadoxine-pyrimethamine in uncomplicated plasmodium falciparum malaria in Kolkata

Authors recruited 100 parasitologically confirmed Plasmodium falciparum cases. Among them, 50 patients were given chloroquine and another 50 patients were given sulphadoxine-pyrimethamine. It was observed that in the Chloroquine group out of 50 patients, 30 (60%) showed adequate clinical and parasitological response (ACPR), 15 (30%) had late treatment failure (LTF) and remaining 5 (10%) were lost during the follow up period (LFU). On the other hand in the SP group out of 50 patients, 46 (92%) showed ACPR and only one (2%) had LTF and 3 patients were LFU. The difference of LTF in Chloroquine and Sulfadoxine-pyrimethamine groups was statistically significant (p value < 0.05). Also there was statistically significant difference of the mean parasite clearance time (PCT) of Chloroquine (82.7 hours) and SP group (61.3 hours).

Comment

There are about 1.5 million cases of malaria annually in India of which around 40%-50% are due to Plamodium falciparum. The present study shows that currently there is widespread resistance to chloroquine in P falciparum in the Eastern part of our country. The World Health Organization recommends a policy change whenever 10% of the malaria episodes prove to be unresponsive to the currently used drug. Accordingly the National Vector Borne Disease Control Program (NVBDCP) in its 2013 guidelines has advocated the use of Artemesnin based combination therapy- Artemether- Lumefantrine (ACT-AL) for the North Eastern states in place of chloroquine and of Artemisinin-based Combination Therapy (ACT-SP i.e. artesunate+sulphadoxine-pyrimethamine) in other states. But the present study showed a very high (92%) response rate to the much cheaper combination of sulphadoxine pyrimethamine alone without artesunate atleast in Kolkata. It is possible that this study may change practice in localities like Kolkata. There is a need for more studies on resistance patterns/response rates to different anti-malarials in different parts of the country, so as to guide the proper selection of agents in a geographically appropriate manner.

Basu A, Saha S, Guha SK. Comparative Study of Effectiveness and Resistance Profile of Chloroquine and Sulfadoxine-Pyrimethamine in Uncomplicated Plasmodium falciparum malaria in Kolkata. J Assoc Physicians India 2015;63:32-7.

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