Journal Scan

Alemtuzumab for patients with relapsing multiple sclerosis after disease modifying therapy: a randomized controlled phase 3 trial

Alemtuzumab is a humanized monoclonal antibody targeting CD52 which causes depletion and repopulation of B and T lymphocytes, leading to long lasting changes in adaptive immunity. In this study patients with relapsing -remitting multiple sclerosis who were refractory to first line treatment were recruited .Authors analyzed relapse data of 202 patients randomized to 44 mcg sc. interferon beta 1a thrice a week and compared these with data from 426 patients receiving 12 mg/day i.v. alemtuzumab for 5 days at baseline and 3 days at 12 months. Follow-up was for 2 years from recruitment. Relapse rates were lower for altemtuzumab group vs. Interferon beta1a group (35% vs. 51%; p, 0.001).20% of the patients on Interferon beta1a had sustained accumulation of disability as compared to a value of only 13% for patients on Alemtuzumab ($p<0.001$). However 77% of patients randomized to alemtuzumab had infections compared to only 66% of those on interferon. None of these were serious or fatal. Other complications include thyroid disorders (16%) and immune thrombocytopenia (1%).

Comment

CD52 is present on the surface of mature lymphocytes, but not on the stem cells from which these lymphocytes are derived. After treatment with alemtuzumab, these CD52-bearing lymphocytes are targeted for destruction. The lymphocyte pool is then regenerated from the stem cells.For this reason it has been used in the treatment of chronic lymphocytic leukemia (CLL), cutaneous T-cell lymphoma (CTCL) and T-cell lymphoma. It has previously shown efficacy in patients with untreated relapsing-remitting multiple sclerosis. The present study demonstrates its superiority to interferon beta 1a, even in patients previously refractory to first line therapy, thereby extending the armamentarium available against this disabling illness . Moreover in this study alemtuzumab also showed disease modifying properties as evidenced by reduced accumulation of disability over two years.This study demonstrates once again that the advent of biologicals has enhanced the scope for targeted therapy at different arms of the innate immune system and on various pathways in cancer development. However all these benefits occur at the cost of infections and triggering of autoimmunity(to thyroid and platelets in this instance); thus the cost benefit ratio has to be individualized.

Coles AJ, Twynman CL, Arnold DL et al. Alemtuzumab for patients with relapsing multiple sclerosis after disease modifying therapy : a randomized controlled phase 3 trial. 2012 Lancet; 380:1829-39.

Metabolic syndrome and risk of Cancer. A systematic review and meta-analysis

Authors analyzed 116 datasets from 43 articles, including 38,940 cases of cancer. In cohort studies in men, the presence of metabolic syndrome was associated with liver (relative risk 1.43, $P < 0.0001$), colorectal (1.25, $P < 0.001$), and bladder cancer (1.10, $P = 0.013$). In cohort studies in women, the presence of metabolic syndrome was associated with endometrial (1.61, $P = 0.001$), pancreatic (1.58, $P < 0.0001$), breast postmenopausal (1.56, $P = 0.017$), rectal (1.52, $P = 0.005$), and colorectal (1.34, $P = 0.006$) cancers. Associations with metabolic syndrome were stronger in women than in men for pancreatic ($P = 0.01$) and rectal ($P = 0.01$) cancers. Stronger associations were recorded in Asian populations for liver cancer ($P = 0.002$), in European populations for colorectal cancer in women ($P = 0.004$), and in U.S. populations (whites) for prostate cancer ($P = 0.001$).

Comment

This study focuses on yet another lethal complication (namely cancer) of the metabolic syndrome apart from its well known causative association with cardiovascular disease and type 2 diabetes mellitus. Sedentary

lifestyle, high calorie "junk food" and increasing age, interacting with underlying genetic factors have created a veritable epidemic of the Metabolic Syndrome with its attendant consequences for the health of the population. Promotion of a healthy lifestyle with emphasis on weight control and regular physical exercise would go a long way in blunting the impact of this epidemic.

Esposito K, Ciodini P, ColaoA, Lenzi A, Guigliano D.Metabolic Syndrome and Risk of Cancer.A Systematic review and Meta-analysis. Diabetes Care 2012;35:2402-10.

Impact of second-line drug resistance on tuberculosis treatment outcomes in the United States: MDR-TB is bad enough

Authors analyzed successful treatment completion and death among second line drug-resistant TB cases in the US national TB surveillance system, 1993-2007 (N = 195?518). They defined four combinations of first-line drug resistance based on isoniazid and rifamycin, and three patterns of second line drug resistance: fluoroquinolones, injectable second line drugs and other oral second line drugs. Thus twelve patterns of combined first and second line drug resistance were discernable. With one exception, every pattern of first line drug resistance with additional resistance to second line drugs had lower proportions of successful treatment completion and higher mortality than cases who had the same pattern of first line drug resistance but no additional second line resistance. However the result was statistically significant only for one pairwise comparison, namely between multidrug resistant tuberculosis patients with combined INH and Rifampicin resistance, with versus without additional resistance to injectable second line drugs ($p<0.005$). Moreover patients with resistance to rifampicin had lower successful treatment completion rates and higher mortality than patients without rifampicin resistance for every corresponding combination of first line drug resistance, both with and without every combination of second line drug resistance. Outcomes were better for human immunodeficiency virus (HIV) negative than HIV-positive cases for all resistance patterns, but improved among HIV-infected cases after 1998, when highly active antiretroviral treatment (HAART) became widely available.

Comment

The worldwide emergence of drug-resistant tuberculosis has focused attention on treatment with second-line drugs .Earlier studies reported that the prevalence of MDR tuberculosis has been shown to vary widely over different regions, with the higher rates being found in Nepal (48%), Gujarat, India (34%), New York city (USA) (30%), Bolivia (15%) and South Korea (15%). This study shows that rifampicin resistance among first line drugs is more unfavourable than isoniazid resistance and or second line drug resistance. Additional second line drug resistance worsens the outlook for patients with MDR TB. Also Introduction of HAART has improved outcomes in drug resistant tuberculosis patients having HIV infection.

Althomsons SP, Cegielski JP. Impact of second-line drug resistance on tuberculosis treatment outcomes in the United States: MDR-TB is bad enough. Int J Tuberc Lung Dis. 2012;16:1331-4.

Mortality of dialysis patients according to influenza and pneumococcal vaccination status

Authors surveyed dialysis centers and performed a retrospective analysis of health status at dialysis therapy initiation, vaccination for influenza and pneumococcal disease, laboratory results, and mortality associated with the 2005-2006 influenza season for patients in three End-Stage Renal Disease Networks across the United States.Of 1,033 dialysis facilities considered, 903 centers with a total patient population of 54,734 reported vaccination data. Analysis was limited to 36,966 patients on dialysis treatment for at least 1 year as of December 31, 2005.Estimated adjusted odds ratio for mortality for patients vaccinated with pneumococcal vaccine alone was 0.77, while that for patients

vaccinated with influenza vaccine alone was 0.73 when compared to unvaccinated patients. Combined vaccination for both influenza and pneumococcus yielded an OR of 0.61 for mortality.

Comment

These results support the vaccine recommendations for patients on chronic dialysis by The Advisory Committee on Immunization Practices and the American Academy of Pediatrics as published in 2000 which recommend pneumococcal vaccination and annual influenza vaccinations (based on the current prevalent strains of influenza virus) for all patients with end stage renal disease who are considered to be immunocompromised.It is well known that an episode of influenza may be complicated by the subsequent development of pneumococcal pneumonia.

Bond TC, Spaulding AC, Krisher J, McClellan W.Mortality of dialysis patients according to influenza and pneumococcal vaccination status. Am J Kidney Dis. 2012;60:959-65.

Reviewers

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