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Search details
Azathioprine and the risk of developing malignancy/cancer

Resources searched
NHS evidence, Cochrane Library, TRIP, Medline, Embase

Summary

Guidelines

Evidence based reviews
From the Cochrane Library:

Azathioprine for multiple sclerosis 2009

Azathioprine for treating rheumatoid arthritis 2009.

Azathioprine or 6-mercaptopurine for induction of remission in Crohn's disease 2009.

Published research
1. Azathioprine, mucosal healing in ulcerative colitis, and the chemoprevention of colitic cancer: A clinical-practice-based forecast

Author(s): Actis G.C., Pellicano R., David E., Sapino A.

Citation: Inflammation and Allergy - Drug Targets, March 2010, vol./is. 9/1(6-9), 1871-5281 (March 2010)

Publication Date: March 2010

Abstract: The development of colorectal cancer in ulcerative colitis is a function of disease duration, with the risk approaching 14% at 25 years. Colitic cancer has become an issue in the last decades, as the availability of effective immune suppressors has reduced resort to curative colectomies. Scrutiny of the available drug options for ulcerative colitis has generated solid evidence of a chemopreventive role of mesalamines. Recent studies on the thiopurines azathioprine and mercaptopurine have unraveled the ability of these drugs to reduce inflammation and influence adaptive immunity by enhancing apoptosis. This evidence, speaking in favor of a chemopreventive role of thiopurines, has not been supported until recently by clinical studies. By contrast, endoscopic and clinical data in our hands have continued to suggest such a role: of a cohort of ulcerative colitis patients treated with azathioprine for 17 years, those on active treatment had no mucosal inflammation on endoscopy and overall none in this cohort developed cancer. This retrospective data have now been validated by cutting-edge information from a prospective nationwide study from an independent group which found a significant chemopreventive effect of azathioprine in those with extended long-standing colitis. Combination of our single-center experience with the data from this large study strongly indicates that the immune modulatory properties of thiopurines can translate into clinically meaningful anti-cancer activity in colitis. These results are likely to influence the medical choices of inflammatory bowel disease caregivers in the decades to come. copyright 2010 Bentham Science Publishers Ltd.

Source: EMBASE


Author(s): Nguyen T, Vacek PM, O'Neill P, Colletti RB, Finette BA

Citation: Cancer Research, September 2009, vol./is. 69/17(7004-12), 0008-5472;1538-7445 (2009 Sep 1)

Publication Date: September 2009

Abstract: The thiopurines azathioprine and 6-mercaptopurine (6-MP) are effective immune modulators and cytotoxic agents extensively used in the treatment of autoimmune diseases, graft rejection, and cancer. There is compelling epidemiologic evidence that thiopurine treatment increases the risk for a variety of tumors by mechanisms that are unclear. We investigated the in vivo mutagenicity of long-term thiopurine treatment by determining the frequency and spectra of somatic mutation events at the hypoxanthine phosphoribosyltransferase (HPRT) locus in peripheral T lymphocytes as well as the prevalence of mutant clonal proliferation in a
cross-sectional analysis of data from 119 children and adults with inflammatory bowel disease (IBD). ANOVA and regression were performed to assess relationships among the frequency and spectra of HPRT mutations with disease, duration of illness, duration of treatment, and total therapeutic dose of azathioprine and 6-MP. We observed a significant increase in the frequency of somatic mutations in 56 subjects treated with thiopurines for IBD compared with 63 subjects not treated with thiopurines. This increase was related to both total dose (P < 0.001) and duration of treatment (P < 0.001). Comparative mutation spectra analysis of 1,020 mutant isolates revealed a significant increase in the proportion of all transitions (P < 0.001), particularly G:C to A:T transitions (P < 0.001). Combined analyses of two signatures for mutant clonality, HPRT mutation, and T-cell receptor beta CDR3 region unique gene sequence also showed a significant thiopurine-dependent increase in mutant cell clonal proliferation (P < 0.001). These findings provide in vivo evidence for mutation induction as a potential carcinogenic mechanism associated with chronic thiopurine intervention.

Source: MEDLINE

Full Text:
Available in fulltext at National Library of Medicine

3. Nodular malignant melanoma and multiple cutaneous neoplasms under immunosuppression with azathioprine.

Author(s): Guenova E, Lichte V, Hoetzenecker W, Woelbing F, Moehrle M, Roecken M, Schaller M

Citation: Melanoma Research, August 2009, vol./is. 19/4(271-3), 0960-8931;1473-5636 (2009 Aug)

Publication Date: August 2009

Abstract: Immunosuppressed patients are at increased risk of skin cancer. A 67-year-old renal transplant recipient developed a nodular malignant melanoma after 30 years of immunosuppression with azathioprine and prednisolone. The patient died of metastatic disease 3 months after the diagnosis was made. The function of the renal graft was not affected at all. Renal transplant recipients are at high risk of developing nonmelanocytic skin tumors when on immunosuppressive therapy with cyclosporine A. Less common is the development of skin cancer during immunosuppression with azathioprine. Latest reports show the increased incidence of malignant melanoma in immunosuppressed patients. Our case illustrates the necessity of close dermatological surveillance of allograft recipients, to assure an early recognition of any malignant skin tumor and to reduce the risk of systemic metastatic disease.

Source: MEDLINE

1. Benign and malignant skin lesions in renal transplant recipients

Citation: Indian Journal of Dermatology, July 2009, vol./is. 54/3(247-250), 0019-5154;1998-3611 (01 Jul 2009)

Publication Date: July 2009

Abstract: Background: Skin lesions - benign and malignant - occur frequently in organ transplant recipients receiving long-term immunosuppressive therapy. These patients are at greater risk of skin cancers. Aims: To study dermatologic problems in renal transplant recipients (RTRs). Methods: One hundred patients (53 men and 47 women) were consecutively examined for benign and malignant skin complications since transplantation in Razi Hospital in Tehran Medical University. The main immunosuppressive therapy regimen in these patients was a combination of prednisolone, azathioprine, and cyclosporine. Results: The early and most common complication was cosmetic side effects that occurred in 98% patients. Skin infections occurred in 83% of the patients and most of them were viral infections (65%), especially of human papilloma viruses (HPVs) in 40% of the patients. We found six cases of malignancy in these patients in that four cases were skin cancers, including one case of SCC, one BCC, and two cases of Kaposi's sarcoma. Dermatologic problems occur most frequently in RTRs, especially skin cancers which have higher frequency in these patients than general population, particularly, Kaposi sarcoma. Sun exposure has an important role in developing epithelial skin cancers following transplantation. The age of developing skin cancer in these patients was early than normal population. Conclusion: Our results emphasize the importance of dermatologic examinations and monitoring RTRs to obtain an early diagnosis and treatment of cutaneous manifestations.

Source: EMBASE

Full Text: Available in fulltext at National Library of Medicine

4. Rapamycin instead of mycophenolate mofetil or azathioprine in treatment of post-renal transplantation urothelial carcinoma

Author(s): Hu X.-P., Ma L.-L., Wang Y., Yin H., Wang W., Yang X.-Y., Zhang X.-D.

Citation: Chinese Medical Journal, January 2009, vol./is. 122/1(35-38), 0366-6999 (05 Jan 2009)

Publication Date: January 2009

Abstract: Background: Malignant tumor is the most common complication occurred in transplant recipients. It is widely recognized that immunosuppressive treatments increase the risk of cancer in transplant recipients. The efficacy and safety of rapamycin (RPM) in combination with low-dose calcineurin inhibitor (CNI) in treating 15 renal allograft recipients which developed urothelial carcinoma were observed. Methods: Immunosuppressive regimen in all recipients was altered with rapamycin to replace mycophenolate mofetil (MMF) or azathioprine (Aza). The initial loading dosage was 2 mg/d, and the next dosage was 1 mg/d. The dosage
of rapamycin was carefully adjusted according to the blood drug level and concentration of the drug was maintained at 4-6 μg/L. In all the 15 patients, the calcineurin inhibitor was reduced down to one third of the original dosage after the rapamycin blood concentration became stable. Surgical treatment and intravesical instillation chemotherapy were carried out in all patients. Recurrence of the tumor was monitored throughout the study. Post-transplant renal function and side effects were also closely monitored. Results: Among the 15 patients, 9 had no tumor recurrence in 2 years, 2 had tumor recurrences twice, and 4 had once. There was no acute rejection observed during RPM treatment. Post-transplant renal function in 11 patients was improved, with a decreased creatinine level. Hyperlipidemia and thrombocytopenia were the most frequent adverse events which responded well to corresponding treatments. Conclusion: Among the renal allograft recipients with urothelial carcinoma, combination of rapamycin and low dose calcineurin inhibitor treatment is effective and safe.

Source: EMBASE

5. Combination of azathioprine and UVA irradiation is a major source of cellular 8-oxo-7,8-dihydro-2'-deoxyguanosine

Author(s): Cooke M.S., Duarte T.L., Cooper D., Chen J., Nandagopal S., Evans M.D.

Citation: DNA Repair, December 2008, vol./is. 7/12(1982-1989), 1568-7864 (01 Dec 2008)

Publication Date: December 2008

Abstract: Thiopurine antimetabolites, such as azathioprine (Aza) and 6-thioguanine (6-TG), are widely used in the treatment of cancer, inflammatory conditions and organ transplantation patients. Recent work has shown that cells treated with 6-TG and UVA generate ROS, with implied oxidatively generated modification of DNA. In a study of urinary 8-oxo-7,8-dihydro-2'-deoxyguanosine (8-oxodG) in renal transplant patients, we provided the first in vivo evidence linking Aza and oxidatively damaged DNA. Using the hOGG1 comet assay, we herein demonstrate high levels of 8-oxodG and alkali-labile sites (ALS) in cells treated with biologically relevant doses of 6-TG, or Aza, plus UVA. This damage was induced dose-dependently. Surprisingly, given the involvement of 6-TG incorporation into DNA in its therapeutic effect, significant amounts of 8-oxodG and ALS were induced in quiescent cells, although less than in proliferating cells. We speculate that some activity of hOGG1 towards unirradiated, 6-TG treated cells, implies possible recognition of 6-TG or derivatives thereof. This is the first report to conclusively demonstrate oxidatively damaged DNA in cells treated with thiopurines and UVA. These data indicate that Aza-derived oxidative stress will occur in the skin of patients on Aza, following even low level UVA exposure. This is a probable contributor to the increased risk of non-melanoma skin cancer in these patients. However, as oxidative stress is unlikely to be involved in the therapeutic effects of Aza, intercepting ROS production in the skin could be a viable route by which this side effect may be minimised. copyright 2008 Elsevier B.V. All rights reserved.

Source: EMBASE
6. Are we giving azathioprine too much time?

**Author(s):** Gomollon F., Lopez Garcia S.

**Citation:** World Journal of Gastroenterology, September 2008, vol./is. 14/36(5519-5522), 1007-9327 (28 Sep 2008)

**Publication Date:** September 2008

**Abstract:** Azathioprine is currently the key drug in the maintenance treatment of inflammatory bowel diseases. However, there are still some practical issues to be resolved: one is how long we must maintain the drug. Given that inflammatory bowel diseases are to date chronic, non-curable conditions, treatment should be indefinite and only the loss of efficacy or the appearance of serious side effects may cause withdrawal. As regards to efficacy and their maintenance over time, evidence supports the continuous usefulness of the drug in the long term: in fact its withdrawal very substantially increases the risk of relapse. About side effects, azathioprine is a relatively well tolerated drug and even indefinite use seems safe. The main theoretical risks of prolonged use would be the myelotoxicity, hepatotoxicity, and the development of cancer. In fact, serious bone marrow suppression or serious liver damage are uncommon, and can be minimized with proper use of the drug. Recent metanalysis suggests that the risk of lymphoma is real, but the individual risk is rather low, and decision analysis suggests a favorable benefit/risk ratio in the long term. Therefore, in patients with inflammatory bowel diseases in whom azathioprine is effective and well tolerated, the drug should not be stopped. This recommendation concerns the use of azathioprine as a single maintenance drug, and is not necessarily applicable to patients receiving concomitant biological therapy. copyright 2008 The WJG Press. All rights reserved.

**Source:** EMBASE

**Full Text:**

Available in fulltext at National Library of Medicine

7. Hematologic malignant neoplasms after drug exposure in rheumatoid arthritis

**Author(s):** Bernatsky S., Clarke A.E., Suissa S.

**Citation:** Archives of Internal Medicine, February 2008, vol./is. 168/4(378-381), 0003-9926;1538-3679 (25 Feb 2008)

**Publication Date:** February 2008

**Abstract:** Background: Rheumatoid arthritis is a severe inflammatory polyarthritis that requires long-term treatment with disease-modifying antirheumatic drugs. There is increasing concern about the influence of rheumatoid arthritis therapy on the risk for hematologic malignant neoplasms. Methods: We used a case-control design nested in a cohort of 23 810 patients with rheumatoid arthritis assembled from administrative databases covering the population of Quebec, Canada. The study was carried out from January 1, 1980, through December 31, 2003. Case
patients having hematologic malignant neoplasms were ascertained from physician billing and hospitalization records; each case patient was matched for age and sex with 10 control subjects. Adjusting for clinical variables and concomitant medications, we used conditional logistic regression to analyze potential associations between disease-modifying antirheumatic drug exposures and risk for hematologic malignant neoplasms. We estimated rate ratios attributable to each disease-modifying antirheumatic drug exposure. Results: During the study, hematologic malignant neoplasms developed in 619 patients, including lymphomas in 346 patients, leukemia in 178 patients, and multiple myelomas in 95 patients. The unadjusted rate ratios for hematologic malignant neoplasms after drug exposures were as follows: methotrexate, 1.18 (95% confidence interval [CI], 0.99-1.40); azathioprine, 1.44 (95% CI, 1.01-2.03); and cyclophosphamide, 2.21 (95% CI, 1.52-3.20). Because biologic agents first appeared in the Regie d’Assurance Maladie du Quebec formulary in 2002, there were few exposures to these drugs. Adjusted estimates suggested that hematologic cancer risk was most elevated after exposure to cyclophosphamide (rate ratio, 1.84; 95% CI, 1.24-2.73). For lymphomas only, the adjusted rate ratio after cyclophosphamide exposure was 2.12 (95% CI, 1.33-3.54). Conclusions: In this large cohort of patients with rheumatoid arthritis, the greatest relative risk for hematologic malignant neoplasms was noted after use of cyclophosphamide. Assessments of risk related to newer and emerging therapies should carefully consider previous and concomitant medication exposures. copyright2008 American Medical Association. All rights reserved.

Source: EMBASE

Full Text:
Available in fulltext at Highwire Press

8. Lupus: Improving long-term prognosis

Author(s): Doria A., Briani C.

Citation: Lupus, 2008, vol./is. 17/3(166-170), 0961-2033 (2008)

Publication Date: 2008

Abstract: Over recent decades short- and medium-term survival has greatly improved in patients affected with systemic lupus erythematosus, but long-term prognosis still remains poor mainly due to complications of the disease and/or its treatment. To improve long-term prognosis in systemic lupus erythematosus, we should try to adopt, early in the disease course, strategies that can contribute to reducing long-term complications, including screening for and prophylaxis against infections, control of risk factors for atherosclerosis, and cancer surveillance. However, in patients with systemic lupus erythematosus all these preventive strategies are often not sufficient. Indeed, two important systemic lupus erythematosus-related factors play a relevant role in all these complications: severe disease manifestations, such as glomerulonephritis and central nervous system involvement, and corticosteroid and cyclophosphamide use. Therefore, to prevent long-term complications, we should try to control disease activity and severity using the lowest effective dosage of these drugs. Moreover,
strategies directed at preventing clinical manifestations in asymptomatic antinuclear antibody-positive individuals or in antiphospholipid antibody-positive systemic lupus erythematosus patients, as well as at preventing severe manifestations in patients with mild systemic lupus erythematosus at the time of the diagnosis should be considered. Copyright 2008 SAGE Publications.

Source: EMBASE

9. Risk of nonmelanoma skin cancer with azathioprine use

Author(s): Maddox J.S., Soltani K.
Citation: Inflammatory Bowel Diseases, 2008, vol./is. 14/10(1425-1431), 1078-0998;1536-4844 (2008)
Publication Date: 2008
Abstract: While often life-saving for many complex diseases, iatrogenic immunosuppression has been associated with life-threatening infections and malignancies. Among these malignancies is skin cancer. Skin cancer is the most common form of cancer in the United States; the nonmelanoma skin cancers have an annual incidence of greater than 1,000,000 people in the US. It is well documented that the risk of nonmelanoma skin cancer (NMSC) is increased in those who are immunosuppressed. While many articles have been published on skin cancer risk in organ transplant recipients, little has been written regarding the incidence of non-melanoma skin cancer in inflammatory bowel disease. A review of the literature of patients who are immunosuppressed for autoimmune disorders, and specifically inflammatory bowel diseases, is discussed, as well as clinical presentations and treatment options. Copyright copyright 2008 Crohn's & Colitis Foundation of America, Inc.

Source: EMBASE


Citation: Annals of the Rheumatic Diseases, January 2008, vol./is. 67/1(74-9), 0003-4967;1468-2060 (2008 Jan)
Publication Date: January 2008
Abstract: OBJECTIVE: To examine if, in systemic lupus erythematosus (SLE), exposure to immunosuppressive therapy (cyclophosphamide, azathioprine, methotrexate) increases cancer risk. METHODS: A case-cohort study was performed within a multi-site international SLE cohort; subjects were linked to regional tumour registries to determine cancer cases occurring after entry into the cohort. We calculated the hazard ratio (HR) for cancer after exposure to an immunosuppressive drug, in models that controlled for other medications (anti-malarial drugs, systemic glucocorticoids, non-steroidal anti-inflammatory drugs (NSAIDs), aspirin),
smoking, age, sex, race/ethnicity, geographic location, calendar year, SLE duration, and lupus damage scores. In the primary analyses, exposures were treated categorically (ever/never) and as time-dependent. RESULTS: Results are presented from 246 cancer cases and 538 controls without cancer. The adjusted HR for overall cancer risk after any immunosuppressive drug was 0.82 (95% CI 0.50-1.36). Age ≥ 65, and the presence of non-malignancy damage were associated with overall cancer risk. For lung cancer (n = 35 cases), smoking was also a prominent risk factor. When looking at haematological cancers specifically (n = 46 cases), there was a suggestion of an increased risk after immunosuppressive drug exposures, particularly when these were lagged by a period of 5 years (adjusted HR 2.29, 95% CI 1.02-5.15). CONCLUSIONS: In our SLE sample, age ≥ 65, damage, and tobacco exposure were associated with cancer risk. Though immunosuppressive therapy may not be the principal driving factor for overall cancer risk, it may contribute to an increased risk of haematological malignancies. Future studies are in progress to evaluate independent influence of medication exposures and disease activity on risk of malignancy.

Source: MEDLINE

Full Text: Available in fulltext at Highwire Press

11. Azathioprine. Safety profile in multiple sclerosis patients

Author(s): La Mantia L., Mascoli N., Milanese C.

Citation: Neurological Sciences, September 2007, vol./is. 28/6(299-303), 1590-1874 (Sep 2007)

Publication Date: September 2007

Abstract: Azathioprine (Aza) has been proposed in the treatment of multiple sclerosis (MS) since 1971 and continues to be used in MS Clinical Centres. Recent data, suggesting its efficacy in reducing MRI lesion load and in refractory IFN-treated MS patients, has renewed interest in this drug. Its therapeutic index over other immunosuppressive agents is generally considered favourable, but concerns about a possible risk of malignancy have limited its use. On the other hand, the occurrence of unexpected adverse events (AEs) in clinical trials in recent years has aroused the interest in the safety profile of the drugs. No systematic review of AEs in patients affected by MS is available. The aim of this study is to review the safety profile of the drug in patients affected by MS, in order to support a correct management of these patients in the clinical practice. The controlled and observational clinical studies published between 1971 and 2007 have been included. The AEs have been registered in ad hoc form and the frequency has been calculated. The risk of cancer and toxicity on reproductive function has been also considered. Gastrointestinal complaints and leukopenia are the most frequent AEs of Aza therapy in MS, occurring in more than 10% of the patients, while infections, allergy, anaemia, thrombocytopenia and pancytopenia are common (>1%-<10%). Pancreatitis is not common (>0.1%-<1%). Most of them are easily managed by dosage adjustment or therapy interruption. The cancer risk increases with the treatment duration and cumulative dose. No data on reproductive
toxicity in MS treated with Aza are available. The safety profile of Aza is acceptable, if strategies for management of expected AEs are adopted, following dosage and treatment duration indications, and if long-term monitoring to evaluate the risk of cancer is warranted. copyright Springer-Verlag Italia 2007.

Source: EMBASE

13. Risk of malignancy in myasthenia gravis patients exposed to azathioprine therapy for a median period of 3 years.

Author(s): Rawoot A, Little F, Heckmann JM

Citation: South African Medical Journal. Suid-Afrikaanse Tydskrif Vir Geneeskunde, December 2006, vol./is. 96/12(1249-51), 0256-9574;0256-9574 (2006 Dec)

Publication Date: December 2006

Source: MEDLINE

4. Conversion From Calcineurin Inhibitors to Everolimus in Kidney Transplant Recipients With Malignant Neoplasia


Citation: Transplantation Proceedings, October 2006, vol./is. 38/8(2453-2455), 0041-1345 (Oct 2006)

Publication Date: October 2006

Abstract: Cancer has been reported to be more common among kidney transplant recipients than waiting-list patients or the general population. Use of anticalcineurin agents and azathioprine are relevant risk factors. Nine renal allograft recipients (seven men and two women) of mean age 67.6 (55-77) years and mean time after transplantation of 30.7 (58-216) months were switched to everolimus-based immunosuppression because of the presence of biopsy-proven malignancies (eight patients) or neurological tacrolimus toxicity (one patient). One patient with posttransplant lymphoproliferative disease also received chemotherapy with a good evolution at 6 months. He showed an initial increase in the protein to creatinine ratio (peak 3.3 mg/mg at 3 months) that was controlled by increasing the enalapril dose. One patient with skin cancer and severe atheromatosis (baseline SCr 2.5 mg/dL, creatinine clearance 17 mL/min, and protein to creatinine ratio 3.2 mg/mg), had cyclosporine and everolimus overlapped for 25 days, showing a continued poor evolution requiring dialysis initiation at 3 months after switch. The other six patients with recurrent skin cancers had good cancer evolution, with no new skin tumors and regression of skin lesions in three, including not biopsied actinic keratosis. Sudden switching from calcineurin inhibitors to everolimus is safe and may be used in long-term transplant recipients with malignancies. In patients with advanced chronic nephropathy this approach appeared to be less beneficial. copyright 2006 Elsevier Inc. All rights reserved.
14. Extrathymic tumors in patients with myasthenia gravis: A 35-year retrospective study

**Author(s):** Wakata N., Sugimoto H., Nomoto N., Konno S., Nakazora H., Nemoto H., Karihara T.

**Citation:** Neurologist, January 2006, vol./is. 12/1(53-55), 1074-7931 (Jan 2006)

**Publication Date:** January 2006

**Abstract:** Objective: Autoimmune diseases are frequently associated with malignant tumor. In addition, prolonged immunosuppression may favor the development of malignancy. While the coincidence of myasthenia gravis and extrathymic tumor has been reported, the risk and features of these tumors are not well understood. Review Summary: We treated 305 patients with myasthenia gravis from 1968-2003, including 48 thymoma cases. Two hundred twenty-nine patients had undergone thymectomy and 76 had not. We examined cancer risk, tumor characteristics, and associations to medications. We encountered 9 cases of extrathymic tumor. Cancer risk in the thymoma cases was 6.3% and 2.3% in the nonthymoma cases, a statistically insignificant difference. Azathioprine was administered to only 14 in this series of patients; however, 2 patients developed cancer. Conclusions: Cancer risk in patients with myasthenia gravis is 2.6%, similar to that of the general population in Japan. We neurologists need to be aware that prolonged immunosuppression may favor the development of malignancy. Copyright copyright 2006 by Lippincott Williams & Wilkins.

15. Medicine: Azathioprine and UVA light generate mutagenic oxidative DNA damage


**Citation:** Science, September 2005, vol./is. 309/5742(1871-1874), 0036-8075;1095-9203 (16 Sep 2005)

**Publication Date:** September 2005

**Abstract:** Oxidative stress and mutagenic DNA lesions formed by reactive oxygen species (ROS) are linked to human malignancy. Clinical treatments inducing chronic oxidative stress may therefore carry a risk of therapy-related cancer. We suggest that immunosuppression by azathioprine (Aza) may be one such treatment. Aza causes the accumulation of 6-thioguanine (6-TG) in patients' DNA. Here we demonstrate that biologically relevant doses of ultraviolet A (UVA) generate ROS in cultured cells with 6-TG-substituted DNA and that 6-TG and UVA are synergistically mutagenic. A replication-blocking DNA 6-TG photoproduct, guanine sulfonate, was bypassed by error-prone, Y-family DNA polymerases in vitro. A preliminary analysis revealed that in five of five cases, Aza treatment was associated with a selective UVA photosensitivity. These findings may partly explain the
prevalence of skin cancer in long-term survivors of organ transplantation.

Source: EMBASE

1. **Outcome of Kaposi’s sarcoma and graft following discontinuation of immunosuppressive drugs in renal transplant recipients**

**Author(s):** Firoozan A., Hosseini Moghaddam S.M.M., Einollahi B., Pour-Reza-Gholi F., Nafar M., Basiri A., Ebrahimi-Rad R.

**Citation:** Transplantation Proceedings, September 2005, vol./is. 37/7(3061-3064), 0041-1345 (Sep 2005)

**Publication Date:** September 2005

**Abstract:** Purpose. Owing to the use of immunosuppressive drugs, renal transplant recipients are at risk for malignancies including Kaposi’s sarcoma (KS). Following the diagnosis, physicians tend to decrease the doses of immunosuppressive drugs to lower tumor progression rate. On the other hand, those who receive lower doses of immunosuppressive drugs are at a higher risk for acute rejection. In this study, we evaluated the outcome of KS on renal allografts following discontinuation or decrease in the doses of drugs. Methods. Since 1984, 14 (nine men and five women) among 2000 cases of renal transplantation have been diagnosed as KS. In 11 patients, cyclosporine was completely discontinued, the dosage was decreased to half of the initial dose in other cases. Except one case, we discontinued either azathioprine or mycophenolate mofetil. Results. During 57 months of follow-up on average, the serum creatinine level remained normal in 10 but increased in four cases. Kidney function deteriorated in two of these four patients at the beginning of study. Three patients died with normal serum creatinine levels. Discontinuation of immunosuppressive drugs caused complete remission of KS in all patients except one who received chemotherapy. Conclusion. Discontinuation of immunosuppressants following the diagnosis of KS caused complete remission of this cancer in almost all patients and seemed to be relatively safe for kidney graft function. copyright 2005 by Elsevier Inc. All rights reserved.

Source: EMBASE

16. **Increased risk of lymphoma among inflammatory bowel disease patients treated with azathioprine and 6-mercaptopurine**

**Author(s):** Kandiel A., Fraser A.G., Korelitz B.I., Brensinger C., Lewis J.D.

**Citation:** Gut, August 2005, vol./is. 54/8(1121-1125), 0017-5749 (Aug 2005)

**Publication Date:** August 2005

**Abstract:** Background: Inflammatory bowel disease (IBD) is commonly treated with immunomodulators such as azathioprine and 6-mercaptopurine (6-MP). Studies examining lymphoma risk in IBD patients treated with these medications have been underpowered and have yielded conflicting conclusions. Aims: The purpose of this meta-analysis was to provide a more precise estimate of the relative risk of lymphoma among IBD patients.
treated with azathioprine or 6-MP. Methods: Studies were included if they were English language, full article, cohort studies specifically designed to evaluate cancer as an adverse outcome of treatment with azathioprine or 6-MP. Pooled standardised incidence ratios were calculated to estimate the relative risk of lymphoma associated with therapy. Heterogeneity was assessed using Poisson regression. Sensitivity analyses examined the influence of individual studies on risk estimate and heterogeneity statistics. Results: Six studies were identified that met our inclusion criteria. When the data were combined across all studies, the pooled relative risk was 4.18 (95% confidence interval 2.07-7.51; 11 observed cases, 2.63 expected). Sensitivity analysis showed that exclusion of any one study had a relatively small effect on the pooled relative risk estimate (range 3.49-5.21) but excluding either the study with the highest or lowest estimated relative risk eliminated the statistically significant heterogeneity. Conclusions: Our data suggest an approximate fourfold increased risk of lymphoma in IBD patients treated with azathioprine/6-MP. The increased risk of lymphoma could be a result of the medications, the severity of the underlying disease, or a combination of the two.

Source: EMBASE

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Azathioprine for multiple sclerosis
1. Casetta¹,
2. G Iuliano²,
3. G Filippini³

J Neurol Neurosurg Psychiatry 2009;80:131-132
Azathioprine (AZA) is an immunosuppressive drug widely prescribed for the treatment of multiple sclerosis (MS) until the first half of the 1990s. It could be an alternative to interferon β because it is less expensive. Concerns about its safety, mainly a possible increased risk of malignancy, have been raised. This systematic review aimed to determine the trade off between the benefits and risks of azathioprine in MS.