Re: Tagamet good for cancer?

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- *From*: Matti Narkia <mna@xxxxxxxx>
- *Date*: Mon, 30 Oct 2006 20:13:17 +0200

On Mon, 30 Oct 2006 09:12:06 −0500, jonboy42@xxxxxxxxx (J W) wrote:

> I've been doing some reading on this heartburn drug and there seems to be a lot of evidence that it has a strong anticancer effect.
>
> Any thoughts on this? Is it something to look at or hooey. If it's hooey, why so.

Tagamet a.k.a. cimetidine is an immunomodulator and potentially useful at least for those people whose T−helper/T−suppressor ratio is too low due to histamine induced T−suppressor cells. Here some information and references about immunomodulatory action of cimetidine:

Evaluation of Histamine2−Receptor−Antagonists (H2−Antagonists)
http://dacc.bsd.uchicago.edu/drug/Bulletins/n1096.html

"H2−antagonists have been found to improve the function of various parts of the immune system.(6,7) There have been anecdotal reports of the usefulness of histamine−antagonists in the treatment of various cancers refractory to standard treatments (eg, lung cancer, malignant melanoma). The proposed mechanism of immunomodulative effects is the inhibition of suppressor T−lymphocyte activity, an increase in interleukin−2 production, and an enhancement of natural killer cell activity. Hahm and colleagues compared the in vitro effects of cimetidine, ranitidine and famotidine on peripheral blood mononuclear cells in normal controls and patients with gastric cancer. They concluded that cimetidine had the strongest and famotidine had the weakest immunomodulating effect. Cimetidine was found to proliferate peripheral blood mononuclear cells and increase cytotoxic capability. Famotidine had no effects on lymphoproliferation and cytotoxicity. Ranitidine and famotidine were also inferior to cimetidine in inhibiting suppressor T−cell activity, increasing interleukin−2 production and enhancing natural killer cell activity. The authors speculated that this difference may be due to the fact that famotidine and ranitidine lack the imidazole nucleus common to histamine and cimetidine."

Griswold DE, Alessi S, Badger AM, Poste G, Hanna N.
Inhibition of T suppressor cell expression by histamine type 2 (H2)
receptor antagonists.
J Immunol. 1984 Jun;132(6):3054−7.
PMID: 6202771 [PubMed − indexed for MEDLINE]
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=6202771&dopt=Abstract

Nanda NK, Nath I.
Characteristics of histamine receptors present on suppressor T cells
in "healthy individuals".
Int J Immunopharmacol. 1985;7(4):587−95.
PMID: 2931386 [PubMed − indexed for MEDLINE]
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2931386&dopt=Abstract

Griswold DE, Alessi S, Badger AM, Poste G, Hanna N.
Differential sensitivity of T suppressor cell expression to inhibition
by histamine type 2 receptor antagonists.
J Immunol. 1986 Sep 15;137(6):1811−5.
PMID: 2875110 [PubMed − indexed for MEDLINE]
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2875110&dopt=Abstract

Kumar A, Cleveland RP.
"Immunoregulatory effects of cimetidine: inhibition of suppressor cell
effector function in vivo".
Immunopharmacol Immunotoxicol. 1988;10(3):327−32.
PMID: 2974050 [PubMed − indexed for MEDLINE]
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2974050&dopt=Abstract

Kumar A.
Cimetidine: an immunomodulator.
DICP. 1990 Mar;24(3):289−95. Review.
PMID: 2138376 [PubMed − indexed for MEDLINE]
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2138376&dopt=Abstract

Brockmeyer NH, Kreuzfelder E, Bluhm C, Shen G, Scheiermann E, Keinecke
HO, Ohnhaus EE.
Immunomodulation of cimetidine in healthy volunteers.
Klin Wochenschr. 1989 Jan 4;67(1):26−30.
PMID: 2522158 [PubMed − indexed for MEDLINE]
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2522158&dopt=Abstract

Gifford RR, Voss BV, Schmidtke JR, Ferguson RM.
Histamine type−2 receptor antagonist immune modulation. I. Increased
cell−mediated cytotoxicity in normal and in down−regulated systems.
Surgery. 1988 Feb;103(2):184−92.
PMID: 2963399 [PubMed − indexed for MEDLINE]
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2963399&dopt=Abstract

Brockmeyer NH, Kreuzfelder E, Guttmann W, Mertins L, Goos M, Ohnhaus
EE.

Cimetidine and the immuno−response in healthy volunteers.
J Invest Dermatol. 1989 Dec;93(6):757−61.
PMID: 2573637 [PubMed − indexed for MEDLINE]
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2573637&dopt=Abstract

Richtsmeier WJ, Eisele D.
In vivo anergy reversal with cimetidine in patients with cancer.
Arch Otolaryngol Head Neck Surg. 1986 Oct;112(10):1074−7.
PMID: 3755977 [PubMed − indexed for MEDLINE]
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=3755977&dopt=Abstract

Flodgren P, Sjogren HO.
Influence in vitro on NK and K cell activities by cimetidine and
indomethacin with and without simultaneous exposure to interferon.
Cancer Immunol Immunother. 1985;19(1):28−34.
PMID: 3844972 [PubMed − indexed for MEDLINE]
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=3844972&dopt=Abstract

Cimetidine may be useful in some type of cancers, for example in certain type of colorectals cancers. In the study below the 64 colorectal cancer patients were treated with surgery and5−fluorouracil. One group additionally received 800 mg/day of cimetidine. The 10−year survival rate was about 85% in the cimetidine group and about 50% un the control group. The difference was statistically significant.

Matsumoto S, Imaeda Y, Umemoto S, Kobayashi K, Suzuki H, Okamoto T.
Cimetidine increases survival of colorectal cancer patients with high
levels of
sialyl Lewis−X and sialyl Lewis−A epitope expression on tumour cells.
Br J Cancer. 2002 Jan 21;86(2):161−7.
PMID: 11870500 [PubMed − indexed for MEDLINE]
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11870500&dopt=Abstract

Abstract:

"Cimetidine has been shown to have beneficial effects in colorectal cancer patients. In this study, a total of 64 colorectal cancer patients who received curative operation were examined for the effects of cimetidine treatment on survival and recurrence. The cimetidine group was given 800 mg day−1 of cimetidine orally together with 200 mg day−1 of 5−fluorouracil, while the control group received 5−fluorouracil alone. The treatment was initiated 2 weeks after the operation and terminated after 1 year. Robust beneficial effects of cimetidine were noted: the 10−year survival rate of the cimetidine group was 84.6% whereas that of control group was 49.8% (P<0.0001). According to our previous observations that cimetidine blocked the expression of E−selectin on vascular endothelium and inhibited the adhesion of cancer cells to the endothelium, we have further stratified the patients according to

the expression levels of sialyl Lewis antigens X (sLx) and A (sLa). We found that cimetidine treatment was particularly effective in patients whose tumour had higher sLx and sLa antigen levels. For example, the 10−year cumulative survival rate of the cimetidine group with higher CSLEX staining, recognizing sLx, of tumours was 95.5%, whereas that of control group was 35.1% (P= 0.0001). In contrast, in the group of patients with no or low levels CSLEX staining, cimetidine did not show significant beneficial effect (the 10−year survival rate of the cimetidine group was 70.0% and that of control group was 85.7% (P=n.s.)). These results clearly indicate that cimetidine treatment dramatically improved survival in colorectal cancer patients with tumour cells expressing high levels of sLx and sLa."

Other references about cimetidine and cancer:

Hayashi A, Kobayashi K, Imaeda Y, Matsumoto S.
[Cimetidine inhibits the adhesion of cancer cells with sialyl Lewis epitope onto the vascular endothelium]
Gan To Kagaku Ryoho. 2003 Oct;30(11):1788−90. Japanese.
PMID: 14619520 [PubMed − indexed for MEDLINE]
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=14619520

Yoshimatsu K, Ishibashi K, Hashimoto M, Umehara A, Yokomizo H, Yoshida K, Fujimoto T, Iwasaki K, Ogawa K.
[Effect of cimetidine with chemotherapy on stage IV colorectal cancer]
Gan To Kagaku Ryoho. 2003 Oct;30(11):1794−7. Japanese.
PMID: 14619522 [PubMed − indexed for MEDLINE]
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=14619522

Kobayashi K, Matsumoto S, Morishima T, Kawabe T, Okamoto T. Cimetidine inhibits cancer cell adhesion to endothelial cells and prevents metastasis by blocking E−selectin expression.
Cancer Res. 2000 Jul 15;60(14):3978−84.
PMID: 10919677 [PubMed − indexed for MEDLINE]
<http://cancerres.aacrjournals.org/cgi/content/full/60/14/3978>

Siegers CP, Andresen S, Keogh JP.
Does cimetidine improve prospects for cancer patients?. A reappraisal of the evidence to date.
Digestion. 1999 Sep−Oct;60(5):415−21. Review.
PMID: 10473965 [PubMed − indexed for MEDLINE]
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10473965&dopt=Abstract

There has been also some doubts that very long term use of cimetidine could be associated with increased risk of some type of cancers.

Cimetedine's patent has already expired. Unfortunately this is bound to prevent or severely restrict investments into its further research

and testing by the private sector. We just have to hope that the public sector picks up the research.

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Matti Narkia
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