

alfa-2a required a dose reduction for thrombocytopenia.¹ That study, however, excluded patients with baseline platelet counts of less than 75,000 per cubic millimeter and hence does not represent the population studied in our trial or the population targeted in ongoing trials.

Of the five patients with baseline platelet counts that were 70,000 or more per cubic millimeter (with the numbers according to study group listed correctly in Table 1 of our article but incorrectly in the legend for Fig. 1), three initiated and completed the antiviral therapy phase (one in the 30-mg group and two in the 75-mg group). Two patients did not enter the antiviral therapy phase: one (in the 30-mg group) did not enter this phase because of an adverse event, and one (in the placebo group) had insufficient platelets for initiation of antiviral therapy.

John G. McHutchison, M.D.

Duke Clinical Research Institute
Durham, NC 27715
mchut001@mc.duke.edu

1. Heathcote EJ, Shiffman ML, Cooksley WGE, et al. Peginterferon alfa-2a in patients with chronic hepatitis C and cirrhosis. *N Engl J Med* 2000;343:1673-80.

DR. BUSSEL AND COLLEAGUES REPLY: In our article, Figure 2D shows that patients not receiving concomitant ITP medications had a good response to eltrombopag alone. When we compared patients who received concomitant ITP medications with

those who did not, the response rates were as follows: placebo, 16.7% vs. 9.5%; 30 mg, 44.4% vs. 20.0%; 50 mg, 72.7% vs. 68.8%; and 75 mg, 60.0% vs. 93.8%. Of the patients receiving concomitant ITP medications (6 in the placebo group [21%], 10 in the group receiving 30 mg of eltrombopag [33%], 12 in the 50-mg group [40%], and 10 in the 75-mg group [36%]), the majority were taking corticosteroids (21%, 33%, 37%, and 32%, respectively). Six patients were receiving danazol (one in the placebo group and five in the group receiving 50 mg of eltrombopag). In four of these five patients in the 50-mg group (each of whom had taken danazol for at least 139 days without a response), platelet counts of 171,000, 369,000, 499,000, and 652,000 per cubic millimeter were achieved. After the patients had discontinued eltrombopag (while they were continuing to receive danazol), the platelet counts decreased to 43,000, 5000, 14,000, and 55,000 per cubic millimeter, respectively, indicating that eltrombopag, not danazol, was responsible for these large increases in platelets.

James B. Bussel, M.D.

Weill Cornell Medical College
New York, NY 10065
jbussel@med.cornell.edu

Nicole L. Stone, Ph.D.

Michael Arning, M.D., Ph.D.

GlaxoSmithKline
Collegeville, PA 19426-0989

Chitinase-like Protein and Asthma

TO THE EDITOR: In their descriptive study of a chitinase-like protein in patients with asthma, Chupp et al. (Nov. 15 issue)¹ report elevated levels of YKL-40 (human cartilage glycoprotein 39 and chitinase 3-like 1) in the serum and lungs of patients with asthma. We measured YKL-40 concentrations in serum before and 24 hours after segmental allergen challenge,² as well as in bronchoalveolar-lavage fluid 10 minutes and 24 hours after segmental allergen challenge, in 13 patients with allergic asthma, using the same enzyme-linked immunosorbent assay (Quidel). YKL-40 concentrations were significantly elevated in serum ($P=0.01$) and even more elevated in bronchoalveolar-lavage fluid ($P=0.003$) 24 hours after allergen challenge (Table 1). In addition, levels of YKL-40

in bronchoalveolar-lavage fluid were positively correlated with eosinophil counts 24 hours after allergen challenge ($r_s=0.768$, $P=0.002$). Although the pathogenetic role of YKL-40 in asthma remains unclear, we extend the data from Chupp et al.¹ by showing that YKL-40 concentrations increase in response to allergen challenge predominantly at the site of allergen deposition.

Michael Kuepper, Ph.D.

Kai Bratke, Ph.D.

J. Christian Virchow, M.D.

University Medical Clinic Rostock
18057 Rostock, Germany
kuepper@med.uni-rostock.de

1. Chupp GL, Lee CG, Jarjour N, et al. A chitinase-like protein in the lung and circulation of patients with severe asthma. *N Engl J Med* 2007;357:2016-27.

Table 1. Characteristics of the Patients and YKL-40 Concentrations in Serum and Bronchoalveolar-Lavage Fluid (BALF) after Segmental Allergen Challenge.*

Patient No.	Sex	Age	Duration of Asthma	Specific IgE	Allergen	Dose	Serum, before Challenge	Serum, after Challenge	BALF, 10 min after Sham Challenge	BALF, 10 min after Allergen Challenge	BALF, 24 hr after Sham Challenge	BALF, 24 hr after Allergen Challenge
			yr	kU/liter		AU				ng/ml		
1	F	20	14	27.5	Birch	53	55	42	<20	<20	<20	28
2	F	25	17	4.0	Birch	30	31	51	20	<20	30	156
3	F	25	2	16.9	<i>Dermatophagoides pteronyssinus</i>	2	88	65	<20	<20	<20	<20
4	F	24	21	5.2	Rye	4	40	46	<20	<20	<20	24
5	M	20	13	18.7	Rye	1150	29	88	27	<20	27	292
6	F	23	3	20.9	Rye	1430	28	352	<20	<20	<20	54
7	F	28	10	6.9	Birch	64	35	58	<20	<20	<20	82
8	M	34	10	30.7	Rye	46	45	140	<20	<20	<20	55
9	M	24	17	66.3	<i>D. pteronyssinus</i>	49	28	38	<20	<20	<20	<20
10	M	24	4	8.3	<i>D. pteronyssinus</i>	71	29	118	<20	<20	<20	119
11	F	22	2	39.6	Rye	340	27	37	<20	<20	<20	77
12	M	24	16	>100.0	Birch	123	39	67	<20	<20	<20	193
13	M	23	4	46.8	<i>D. pteronyssinus</i>	2180	38	114	<20	<20	<20	31
Median (range)							35 (27–88)	65 (37–352)	<20 (<20–27)	<20	<20 (<20–30)	55 (<20–292)
P value							0.01			0.18		0.003

* AU denotes allergen unit. The detection limit of the enzyme-linked immunosorbent assay was 20 ng per milliliter. P values, which are for the difference in YKL-40 (human cartilage glycoprotein 39 and chitinase 3–like 1) concentrations before and after challenge, were calculated by means of a two-sided Wilcoxon signed-rank test for paired samples, with the use of SPSS software. P values of less than 0.05 were considered to indicate statistical significance.

2. Lommatzsch M, Julius P, Kuepper M, et al. The course of allergen-induced leukocyte infiltration in human and experimental asthma. *J Allergy Clin Immunol* 2006;118:91-7.

THE AUTHORS REPLY: Kuepper et al. present their data showing that YKL-40 levels in bronchoalveolar-lavage fluid and serum increased after segmental antigen challenge. Their data also show that similar responses were induced by antigens that contain chitin and antigens that do not contain chitin. These are interesting findings that support our contention that serum YKL-40 levels

can be increased by localized pulmonary inflammation and our observation that serum YKL-40 levels can reflect ongoing pulmonary asthma responses. Taken together with the results of our study, these findings suggest that persistently elevated circulating YKL-40 levels may be a marker of ongoing antigen-driven inflammation and remodeling in the asthmatic airway.

Geoff Chupp, M.D.

Jack A. Elias, M.D.

Yale University School of Medicine
New Haven, CT 06520

Chemotherapy in Unresectable Head and Neck Cancer

TO THE EDITOR: Radiotherapy alone in patients with advanced head and neck cancer is not the treatment of choice, even when cisplatin, fluorouracil, and docetaxel (TPF) are given. Vermorken et al. (Oct. 25 issue)¹ report that TPF improved progression-free and overall survival in patients with unresectable head and neck cancer, but their results are disappointing as compared with chemoradiotherapy^{2,3} or radiotherapy with cetuximab.⁴ In the same issue, Posner et al. also report better results in patients with advanced head and neck cancer when TPF was combined with radiotherapy.⁵

Edwin Bölke, M.D.

Matthias Peiper, M.D.

Stephan Gripp, M.D.

University of Düsseldorf
40225 Düsseldorf, Germany
boelke@med.uni-duesseldorf.de

1. Vermorken JB, Remenar E, van Herpen C, et al. Cisplatin, fluorouracil, and docetaxel in unresectable head and neck cancer. *N Engl J Med* 2007;357:1695-704.

2. Budach W, Hehr T, Budach V, Belka C, Dietz K. A meta-analysis of hyperfractionated and accelerated radiotherapy and combined chemotherapy and radiotherapy regimens in unresected locally advanced squamous cell carcinoma of the head and neck. *BMC Cancer* 2006;6:28.

3. Brizel DM, Esclamado R. Concurrent chemoradiotherapy for locally advanced, nonmetastatic, squamous carcinoma of the head and neck: consensus, controversy, and conundrum. *J Clin Oncol* 2006;24:2612-7.

4. Bonner JA, Harari PM, Giralt J, et al. Radiotherapy plus cetuximab for squamous-cell carcinoma of the head and neck. *N Engl J Med* 2006;354:567-78.

5. Posner MR, Hershock DM, Blajman CR, et al. Cisplatin and fluorouracil alone or with docetaxel in head and neck cancer. *N Engl J Med* 2007;357:1705-15.

THE AUTHOR REPLIES: We agree with Bölke et al. that radiotherapy alone as locoregional treatment is usually not the treatment of choice for locoregionally advanced head and neck cancer. This is also clearly indicated in the second paragraph of our article. We also state that accelerated or hyperfractionated radiotherapy regimens, which have recently been shown to be superior to conventionally fractionated radiotherapy, were used in only a minority of patients, because at the time our trial started, these standards had not been universally accepted within the European Organization for Research and Treatment of Cancer (EORTC) Head and Neck Cancer Group. However, we would caution against cross-trial comparisons, because patient and tumor characteristics can vary widely.

Jan B. Vermorken, M.D., Ph.D.

Antwerp University Hospital
2650 Edegem, Belgium
jan.b.vermorken@uza.be