

# blood

1993 81: 869-870

## Plasma cell acid phosphatase in multiple myeloma [letter; comment]

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## PLASMA CELL ACID PHOSPHATASE IN MULTIPLE MYELOMA

To the Editor:

In a recent issue of *Blood*, Saeed et al<sup>1</sup> reported about the prognostic significance of plasma cell acid phosphatase (PCAP) in a large number of patients with multiple myeloma, showing that a low PCAP score (<130) at diagnosis might recognize a subgroup of myelomatous patients with poor prognosis.

I believe that such findings are quite surprising in view of the previously published cumulative data on this topic, including personal experience,<sup>2</sup> and of some biologic considerations.

The same group had found a direct correlation between a high PCAP score and "active" phases of disease in selected myelomatous patients<sup>3</sup>; our studies had confirmed these observations.<sup>2</sup> In addition, such as emerged also in the report in discussion, MGUS and "reactive" bone marrow plasmacytosis usually evidence lower PCAP activity than that measured in "overt" myeloma; overlaps may occur, but only at low levels of PCAP score. Finally, in multiple myeloma, a direct correlation between PCAP and plasma cell proliferative activity (one of the most important prognostic factors in this disease), has been reported.<sup>4,5</sup> All of these findings indicate a possible relationship between high levels of PCAP and intrinsic biologic "aggressiveness" of myeloma cells, a fact that seems to contrast with the conclusions of Saeed et al.

Even when we have recently reevaluated PCAP in 102 cases of multiple myeloma adopting the modified scoring method proposed by these investigators, we obtained a good correlation between high PCAP score at diagnosis and poor prognosis (PCAP score >200 v <200: median overall survival 18 v 59 months, respectively,  $P < .001$ ). In particular, increased levels of PCAP were detected in three cases of plasma cell leukemia with very short survival.

As reported previously,<sup>2</sup> we found that the only group of myelomatous subjects who showed a poor clinical outcome associated with a constantly low PCAP score was confined to those patients with a high percentage (>40%) of "flaming" plasma cells. We speculated that the large amount of glycoproteins that is present in these cells could mask the positivity of the cytochemical reaction or, in turn, that the wider cytoplasm extension could lead to a lower total score

for PCAP. In this setting, it is noteworthy that the prognosis of multiple myeloma with "flaming" morphologic features has sometimes been reported to be unfavorable (and overall survival of such cases in our series was significantly lower than that of other patients). It would be of interest to know whether Saeed et al looked at this phenomenon.

In conclusion, in view of the contrasting data at present time available on this topic, I believe that the clinical significance of PCAP in multiple myeloma, if any, remains unclear.

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## RESPONSE

The "surprise" expressed by Dr Musto is understandable since we started our prospective, double-blind study with similar hypotheses and expectations that are expressed in his letter. Most of the questions raised by Dr Musto have already been discussed in our report and the answers should be evident from the data presented.<sup>1</sup> For the most part the published "cumulative" data on plasma cell acid phosphatase (PCAP) deals with the use of PCAP as a differential diagnostic test for multiple myeloma versus monoclonal gammopathy or reactive plasmacytosis.<sup>2-13</sup> Our data support the published conclusions in that regard. The reports by Battallie et al<sup>14</sup> and Musto et al<sup>15</sup> hypothesized about the relationship of PCAP to remission, relapse, and progression of the disease, but neither study provided comprehensive analyses of the prognostic relationship between PCAP and multiple myeloma. Our data was very rigorously examined by univariate, bivariate, and multivariate analyses, and PCAP level less than 130 was consistently associated with poor prognosis.

Dr Musto states that they rescored their myeloma cases and obtained good correlation between high PCAP and poor prognosis. He does not state whether they used stored unstained slides or previously stained slides. As mentioned in our report,<sup>1</sup> we recommend staining the slides within 1 to 2 weeks of bone marrow aspiration; otherwise the results could be unreliable. Previously stained and stored slides can have considerable leaching out of the stained PCAP crystals, producing false results. Dr Musto's statement about prognostic relationship of PCAP in myeloma is intriguing, but the information is too sketchy for us to comment upon.

According to Dr Musto, low PCAP can be associated with high percentage of "flaming" plasma cells. Hoffman et al<sup>13</sup> describe low PCAP in lymphoplasmacytic immunocytomas. In our experience, low PCAP scores do not have predilection for any particular morphologic type. We did not specifically try to correlate the presence of flaming cells and PCAP. When slides stained for PCAP are examined, it is not possible to distinguish flaming plasma cells from other plasma cells. However, flaming plasma cells are most frequently associated with IgA myelomas. Therefore, lower PCAP scores would be expected in IgA myelomas, if Dr Musto's hypothesis is valid. We examined the data in our study and Table 1 shows the range of PCAP scores for different types of myeloma. It is evident that there is no significant difference in the scores for the various myeloma types ( $P = .08$ ). Interestingly, similar lack of correlation between PCAP and M-component types was mentioned by Musto et al.<sup>15</sup>

To conclude, we encourage additional prospective studies of the role of PCAP in myeloma biology, its prognostic impact, and its use as a tool for stratification of patients in myeloma trials.

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**Table 1. Distribution of Plasma Cell Acid Phosphatase Scores According to M-Component in 399 Myeloma Patients**

Disease	N	Mean	Range
IgG- $\kappa$	138	195	89-326
IgG- $\lambda$	70	192	42-355
IgG-unknown	11	181	111-279
IgA- $\kappa$	45	199	99-311
IgA- $\lambda$	32	190	107-263
IgA-unknown	7	166	88-304
BJ only- $\kappa$	46	178	95-305
BJ only- $\lambda$	37	168	95-289
Nonsecretory	7	227	114-395
Other	6	166	104-282