

to him that I would be willing to carry out a clinical trial if you felt this was promising.

As far as compensation for the work done, I feel a grant of \$1500.00 would be fair if you so see fit.

I am sorry you have been too busy to come in to this area. I will be at the American College of Allergy meeting in Miami the first of March. If you have that in your plans I will be happy to see you then. Best regards from Elaine. Hope all is well with you.

Very truly yours,

PAUL CHERVINSKY, M.D.

MINNEAPOLIS, MINN.,
June 24, 1963.

NELSON R. CANTWELL, M.D.,
Merck Sharp & Dohme Laboratories,
West Point, Pa.

DEAR NELSON: I have gone over the data on the 63 patients I reported to you earlier this month and have extracted the information you recently asked about.

1. 40 patients have been on 150 mg or less of Indocin per day. 20 of these reported no or slight help and 20 reported significant (25% to 50%) or great (more than 50%) help.

2. 15 patients had 200 mg per day and 7 reported no or slight help and 8 reported significant to great help.

3. 8 patients had more than 200 mg per day. 5 reported no or slight help and 3 reported significant or great help.

4. All patients had rheumatoid arthritis.

5. There was a definite increase in GI symptoms and especially headache with increase in dosage. There was very little headache on 100 mg or less per day. Gastric irritation seems to be an increasing problem.

6. I have had little experience with non-rheumatoids so far, but 1 patient with Reiter's disease had an excellent response; 1 patient with chronic gout had a good response and 1 patient with Scleroderma had slight help.

7. Regarding headache and migraine; the very day you called, the first patient I asked the question of stated that she had been a frequent sufferer of migraine before developing her arthritis. She had been free of headache until it recurred with Indocin. However, she stated this headache was different from what she remembered her migraine was like. I haven't had the opportunity to put the question to all patients, but several have denied previous migraine, yet 3 have admitted to prior migraine.

8. 39 of the 63 patients have been on Indocin for 2 months or more, some over 8 months. It is my plan to carry as many on long-term therapy as tolerate and benefit from the drug. New patients are being constantly added as I presume is your desire.

Sincerely,

PAUL J. BILKA, M.D.

PAUL J. BILKA, M.D.,
Minneapolis, Minn., August 29, 1962.

NELSON H. REAVEY CANTWELL, M.D.
Merck Sharp & Dohme Research Laboratories,
West Point, Pa.

DEAR DR. CANTWELL: During the last month I have been carrying on a new trial with MK-615 using the higher dosage range which you suggested. A preliminary analysis of 22 patients indicates rather significant improvement in the results using this higher dosage. All patients have rheumatoid arthritis, and the majority have been on the lower dosage trial. The results after 2 to 4 weeks therapy are as follows:

Four patients report no significant improvement.

Five patients report 10 to 25 percent subjective improvement.

Twelve patients report 25 to 50 percent improvement.

One patient reports marked, or over 50 percent improvement.

There have been 2 complaints of nausea caused by the higher dosage and one patient who had a previous active duodenal ulcer, and also is on 0.6mg beta dexamethasone per day developed an active DU on 100mg MK-615 per day. One other patient complained of headaches. I have not, as yet, analysed the laboratory data, but will do this shortly when I fill out the regular investigative forms. I thought, however, that you would be interested in these preliminary findings.

Sincerely,

PAUL J. BILKA, M.D.