CRYSTAL ARTHRITIS

Arhalofenate safely prevents gout flare

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Phase IIb study results just published suggest that arhalofenate can safely prevent flare as well as reduce serum urate levels in patients with gout. This dual mode of action of arhalofenate confers a substantial advantage over other urate-lowering therapies, which initially increase the risk of flare (owing to mobilization of stored urate and shrinkage of intra-articular urate crystals, which facilitates their phagocytosis and causes an inflammatory response).

“All of a sudden we were killing two birds with one stone,” Pol Boudes, corresponding author of the study, comments. “IL-1 β is the cytokine that is key to triggering gout flare,” he continues. “The demonstration (in mice) that arhalofenate was acting as a brake on local release of IL-1 β following an inflammatory challenge with urate crystals was very relevant to making this drug an ideal candidate for gout.”

The 239 participants in this double-blind 12-week multicentre study were patients with ≥ 3 gout

flares during the previous year, who were not taking colchicine or urate-lowering therapy, and had baseline serum uric acid levels 7.5–12.0 mg/dl. They were randomly assigned (2:2:2:2:1) to once-daily arhalofenate 600 mg or 800 mg, allopurinol 300 mg, allopurinol 600 mg plus colchicine 0.6 mg, or placebo. Flare incidence (the number of flares per group divided by the total time of diary data available) was significantly lower in the high-dose arhalofenate group (0.66) than in the allopurinol-only group (1.24, $P=0.0056$) or the placebo group (1.13, $P=0.0049$), and similar to that in the allopurinol plus colchicine group (0.40, $P=0.091$).

Arhalofenate 600 mg resulted in a nonsignificant 16% reduction in flare incidence versus allopurinol. A novel interactive electronic diary was used to record flare episodes. “Gout flares have been evaluated very subjectively in clinical trials up to now, mostly with recall interviews,” comments Boudes. “The e-diary gathers information on physical signs, symptoms and pain medication, which allows us to define and quantify flares very precisely.”

Boudes and colleagues are now planning phase III studies of arhalofenate in combination with febuxostat. “Gout is currently very poorly managed; I would say it is a ‘neglected’ disease,” says Boudes. “If the phase III studies are successful, we think this combination treatment should significantly improve the management of gout.”

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