

Fig. S1. Azathioprine metabolism (summarized) and the shift towards 6-thioguanine nucleotide (6-TGN) production after the addition of allopurinol (red crosses and green arrows). 6-MMP: methylated 6-methylmercaptopurine; HGPRT: hypoxanthine-guanine phosphoribosyl transferase; TPMT: thiopurine methyltransferase; XO: xanthine oxidase. Although the exact mechanism of action of allopurinol co-prescription remains unclear, there are a few proposed mechanisms (4, 12, 13). Competitive inhibition of xanthine oxidase with allopurinol results in an increase in the bioavailability of the active metabolites.(12). It has also been suggested that allopurinol may inhibit TPMT by the production of metabolite 6-thioxanthine (6-TX) (12, 14, 15). Another mechanism involves increased activity of HGPRT towards the active pathway (12, 14, 16).