**Supplementary Table 4.** Results of secondary multivariate Cox-proportional Hazard analysis to calculate the Hazard ratio for AZA and MP for the risk of adverse events adjusted for thiopurine dose and week eight metabolite levels.

|  |  |  |  |
| --- | --- | --- | --- |
| Adverse event | Hazard Ratio (95% CI interval) | p-value | Cases and controls included in the analysis |
| Hepatotoxicity | 1.65 (0.56-4.84) | 0.36 | 19 cases, 136 controls |
| Leukopenia | 2.28 (0.54-9.61) | 0.26 | 11 cases, 143 controls |
| Gastrointestinal side effects | 1.28 (0.72-2.29) | 0.40 | 62 cases, 93 controls |
| Treatment response | 0.77 (0.22-2.75) | 0.70 | 84 patients included |

Analyses were identical to the secondary analyses presented in the main text, with the difference that week eight 6-MMPR and 6-TGN levels were used instead of week one metabolite levels. The rationale behind this is that most cases of hepatotoxicity and leukopenia occurred before week eight and as a consequence most patients stopped treatment or were subjected to dose reductions. Therefore, week eight metabolite levels were either not available or levels were not representative in the majority of the cases. For this reason secondary analyses with week one levels were more representative and in addition more patients could be included. The results presented in this supplementary file corroborate those from the main text, indicating that the significant higher rates of hepatotoxicity and leukopenia in the univariate analysis in patients on MP do not stand in a secondary analysis with adjustment for the relative higher dose and higher metabolite levels in patients on MP compared to AZA.

6-MMPR, 6-methylmercaptopurine ribonucleotides; 6-TGN, 6-thioguanine nucleotides; AZA, azathioprine; CI, Confidence Interval; MP, mercaptopurine