SUPPLEMENTARY MATERIAL

Supplementary methods

R packages (R v.4.4.1) used in analysis:

- MissForest: Used for imputation of missing values using a random forest algorithm. Stekhoven DJ, Buhlmann P. MissForest--non-parametric missing value imputation for mixed-type data. Bioinformatics. 2012;28(1):112-8.
- lmtest: Used for carrying out likelihood ratio testing between backward stepwise regression models. Hothorn T, Zeilis A, Farebrother RW, Cummins C, Millo G, Mitchell D. lmtest: Testing Linear Regression Models 2022 [Available from: https://CRAN.R-project.org/package=lmtest.
- mlr3: Used for carrying out resampling of the final model using out-of-bag bootstrapping, to assess model performance and to generate ROC curves of resampling results. Lang M, Binder M, Richter J, Schratz P, Pfisterer F, Coors S, et al. mlr3: A moden object-oriented machine learning framework in R. Journal of Open Source Software. 2019;4(44):1903-5.

FBC components excluded from analysis, with rationale:

- Total white cell count – this is a composite value of all the differential white cells already analysed, so was excluded to prevent duplication of data already included in analysis.
- Basophils – this component had near-zero variance so was excluded as it was likely to be an uninformative predictor.

Supplementary tables

Table S1. Univariable linear regression of pre-treatment FBC components and tender joint count of 28 joints after six months of treatment with a bDMARD.

FBC component	**Univariable analysis**		**Adjusted for potential confounders**	
	β-coefficient (95% CI)	*p-value*	*β-coefficient$_{adj}$ (95% CI)*	*p-value*
Haemoglobin, per g/dL	-4.91E-03 (-0.03 – 0.02)	0.74	-0.01 (-0.04 – 0.02)	0.68
Haematocrit, per unit	-0.05 (-0.13 – 0.02)	0.15	-0.02 (-0.11 – 0.07)	0.72
Mean cell volume, per fL	0.03 (-0.05 – 0.11)	0.46	0.01 (-0.08 – 0.10)	0.85
Platelets, per 10E09/L	1.08E-03 (-4.24E-03 – 0.01)	0.69	3.96E-04 (-0.01 – 0.01)	0.90
Neutrophils, per 10E09/L	0.23 (-0.01 – 0.47)	0.06	0.16 (-0.10 – 0.43)	0.23
Lymphocytes, per 10E09/L	-0.12 (-0.96 – 0.73)	0.79	-0.21 (-1.06 – 0.64)	0.63
Eosinophils, per 10E09/L	0.93 (-3.18 – 5.04)	0.66	0.83 (-3.27 – 4.93)	0.69
Monocytes, per 10E09/L	1.71 (-0.64 – 4.07)	0.16	1.26 (-1.29 – 3.80)	0.34

Abbreviations: Adjusted (adj), biologic DMARD (bDMARD), confidence intervals (CI), full blood count (FBC), odds ratio (OR).

Table S2. Univariable linear regression of pre-treatment FBC components and swollen joint count of 28 joints after six months of treatment with a bDMARD.

FBC component	**Univariable analysis**		**Adjusted for potential confounders**	
	β-coefficient (95% CI)	*p-value*	*β-coefficient$_{adj}$ (95% CI)*	*p-value*
Haemoglobin, per g/dL	-1.92E-03 (-0.02 – 0.02)	0.84	-1.99E-03 (-0.02 – 0.02)	0.84
Haematocrit, per unit	-0.03 (-0.08 – 0.02)	0.19	-3.70E-03 (-0.06 – 0.05)	0.90
Mean cell volume, per fL	-0.03 (-0.08 – 0.02)	0.23	-0.03 (-0.09 – 0.03)	0.32
Platelets, per 10E09/L	2.73E-03 (-5.74E-04 – 0.01)	0.11	1.72E-03 (-2.03E-03 – 0.01)	0.37
Neutrophils, per 10E09/L	0.11 (-0.04 – 0.26)	0.15	0.06 (-0.11 – 0.23)	0.49
Lymphocytes, per 10E09/L	-0.01 (-0.53 – 0.52)	0.98	0.01 (-0.52 – 0.55)	0.96
Eosinophils, per 10E09/L	1.57 (-0.99 – 4.12)	0.23	1.38 (-1.21 – 3.97)	0.30
Monocytes, per 10E09/L	1.56 (0.10 – 3.03)	0.04*	1.47 (-0.14 – 3.07)	0.07

*Indicates $p<0.05$.

Abbreviations: Adjusted (adj), biologic DMARD (bDMARD), confidence intervals (CI), full blood count (FBC), odds ratio (OR).

Table S3. Univariable linear regression of pre-treatment FBC components and patient global health (visual analogue scale, 0 – 100mm) after six months of treatment with a bDMARD.

FBC component	**Univariable analysis**		**Adjusted for potential confounders**	
	β-coefficient (95% CI)	*p-value*	*β-coefficient$_{adj}$ (95% CI)*	*p-value*
Haemoglobin, per g/dL	-0.02 (-0.18 – 0.14)	0.82	-0.01 (-0.18 – 0.16)	0.89
Haematocrit, per unit	-0.24 (-0.65 – 0.16)	0.24	0.02 (-0.49 – 0.53)	0.94
Mean cell volume, per fL	-0.03 (-0.48 – 0.42)	0.90	-0.17 (-0.67 – 0.34)	0.52
Platelets, per 10E09/L	0.01 (-0.02 – 0.04)	0.43	0.01 (-0.03 – 0.04)	0.69
Neutrophils, per 10E09/L	1.01 (-0.32 – 2.35)	0.14	0.84 (-0.67 – 2.34)	0.28
Lymphocytes, per 10E09/L	0.08 (-4.61 – 4.77)	0.97	-1.17 (-5.95 – 3/61)	0.63
Eosinophils, per 10E09/L	1.66 (-21.20 – 24.51)	0.89	3.83 (-19.24 – 26.91)	0.75
Monocytes, per 10E09/L	9.67 (-3.41 – 22.76)	0.15	8.33 (-5.98 – 22.66)	0.26

Abbreviations: Adjusted (adj), biologic DMARD (bDMARD), confidence intervals (CI), full blood count (FBC), odds ratio (OR).

Table S4. Univariable linear regression of pre-treatment FBC components and high-sensitivity CRP after six months of treatment with a bDMARD.

FBC component	**Univariable analysis**		**Adjusted for potential confounders**	
	β-coefficient (95% CI)	*p-value*	*β-coefficient$_{adj}$ (95% CI)*	*p-value*
Haemoglobin, per g/dL	-0.16 (-0.34 – 0.02)	0.08	-0.16 (-0.35 – 0.02)	0.09
Haematocrit, per unit	-0.22 (-0.67 – 0.23)	0.33	-0.14 (-0.70 – 0.42)	0.62
Mean cell volume, per fL	-0.22 (-0.72 – 0.27)	0.38	-0.12 (-0.67 – 0.43)	0.66
Platelets, per 10E09/L	0.04 (0.01 – 0.07)	0.01*	0.02 (-0.01 – 0.06)	0.20
Neutrophils, per 10E09/L	2.00 (0.56 – 3.45)	0.01*	1.38 (-0.26 – 3.01)	0.10
Lymphocytes, per 10E09/L	3.37 (-1.75 – 8.48)	0.20	2.81 (-2.40 – 8.01)	0.29
Eosinophils, per 10E09/L	22.65 (-2.19 – 47.50)	0.08	22.82 (-2.18 – 47.82)	0.08
Monocytes, per 10E09/L	21.63 (7.52 – 35.73)	2.96E-03*	18.07 (2.58 – 33.55)	0.02*

*Indicates $p<0.05$.

Abbreviations: Adjusted (adj), biologic DMARD (bDMARD), confidence intervals (CI), full blood count (FBC), odds ratio (OR).

Table S5. Univariable linear regression of pre-treatment FBC components and DAS28-CRP after six months of treatment with a bDMARD.

FBC component	**Univariable analysis**		**Adjusted for potential confounders**	
	β-coefficient (95% CI)	*p-value*	*β-coefficient$_{adj}$ (95% CI)*	*p-value*
Haemoglobin, per g/dL	-4.41E-03 (-0.01 – 4.42E-03)	0.33	-4.18E-03 (-0.01 – 4.83E-03)	0.36
Haematocrit, per unit	-0.02 (-0.04 – 1.07E-03)	0.06	-0.01 (-0.03 – 0.02)	0.64
Mean cell volume, per fL	-0.01 (-0.03 – 0.02)	0.47	-0.01 (-0.04 – 0.01)	0.28
Platelets, per 10E09/L	1.35E-03 (-2.44E-04 – 2.94E-03)	0.10	8.76E-04 (-8.88E-04 – 2.64E-03)	0.33
Neutrophils, per 10E09/L	0.11 (0.04 – 0.18)	2.85E-03*	0.09 (0.01 – 0.17)	0.03*
Lymphocytes, per 10E09/L	-0.01 (-0.27 – 0.24)	0.92	-0.04 (-0.30 – 0.21)	0.73
Eosinophils, per 10E09/L	0.28 (-0.96 – 1.51)	0.66	0.26 (-0.96 – 1.48)	0.68
Monocytes, per 10E09/L	0.87 (0.17 – 1.58)	0.02*	0.74 (-0.01 – 1.50)	0.05

*Indicates $p<0.05$.

Abbreviations: Adjusted (adj), biologic DMARD (bDMARD), confidence intervals (CI), full blood count (FBC), odds ratio (OR).

Table S6. Univariable logistic regression of pre-treatment FBC components and EULAR non-response after six months of treatment with a bDMARD.

FBC component	*Unadjusted univariable analysis*		*Adjusted for confounders*	
	OR (95% CI)	**p-value**	**OR_{adj} (95% CI)**	**p-value**
Haemoglobin, per g/dL	1.01 (0.99 – 1.03)	0.30	1.02 (0.99 – 1.05)	0.13
Haematocrit, per unit	0.83 (0.26 – 2.58)	0.74	0.89 (0.41 – 1.93)	0.76
MCV, per fL	1.01 (0.96 – 1.06)	0.69	1.02 (0.95 – 1.09)	0.56
Platelets, per 10E09/L	1.00 (1.00 – 1.00)	0.62	1.00 (0.99 – 1.00)	0.59
Neutrophils, per 10E09/L	0.99 (0.85 – 1.15)	0.92	1.04 (0.95 – 1.27)	0.71
Lymphocytes, per 10E09/L	0.91 (0.53 – 1.55)	0.72	0.84 (0.45 – 1.56)	0.58
Eosinophils, per 10E09/L	12.00 (1.16 – 124.38)	0.04*	23.40 (1.38 – 397.39)	0.03*
Monocytes, per 10E09/L	8.46 (2.01 – 35.62)	3.62E-03*	13.94 (2.15 – 90.20)	0.01*

*Indicates $p<0.05$.

Abbreviations: Adjusted (adj), biologic DMARD (bDMARD), confidence intervals (CI), full blood count (FBC), odds ratio (OR).

Table S7. Comparison between model performance monocytes with covariates vs covariates alone after six months of treatment with a bDMARD.

Performance measure	**Monocytes with covariates model**	**Covariates only model**
Classification error (%)	20.32	19.20
Classification accuracy (%)	79.68	80.80
AUROC (%)	60.42	58.47
AIC	184.36	188.51

Abbreviations: Akaike information criterion (AIC), area under the receiver operating characteristic curve (AUROC), biologic DMARD (bDMARD).

Supplementary Figures

Supplementary Figure 1. Comparison of absolute monocyte counts between responders and non-responders, and with normal reference range.