Web extra material (Appendix)

Maintenance treatment with the immunomodulator MGN1703, a toll-like receptor 9 (TLR9) agonist, in patients with metastatic colorectal carcinoma and disease control after chemotherapy: a randomised, double-blind, placebo-controlled trial

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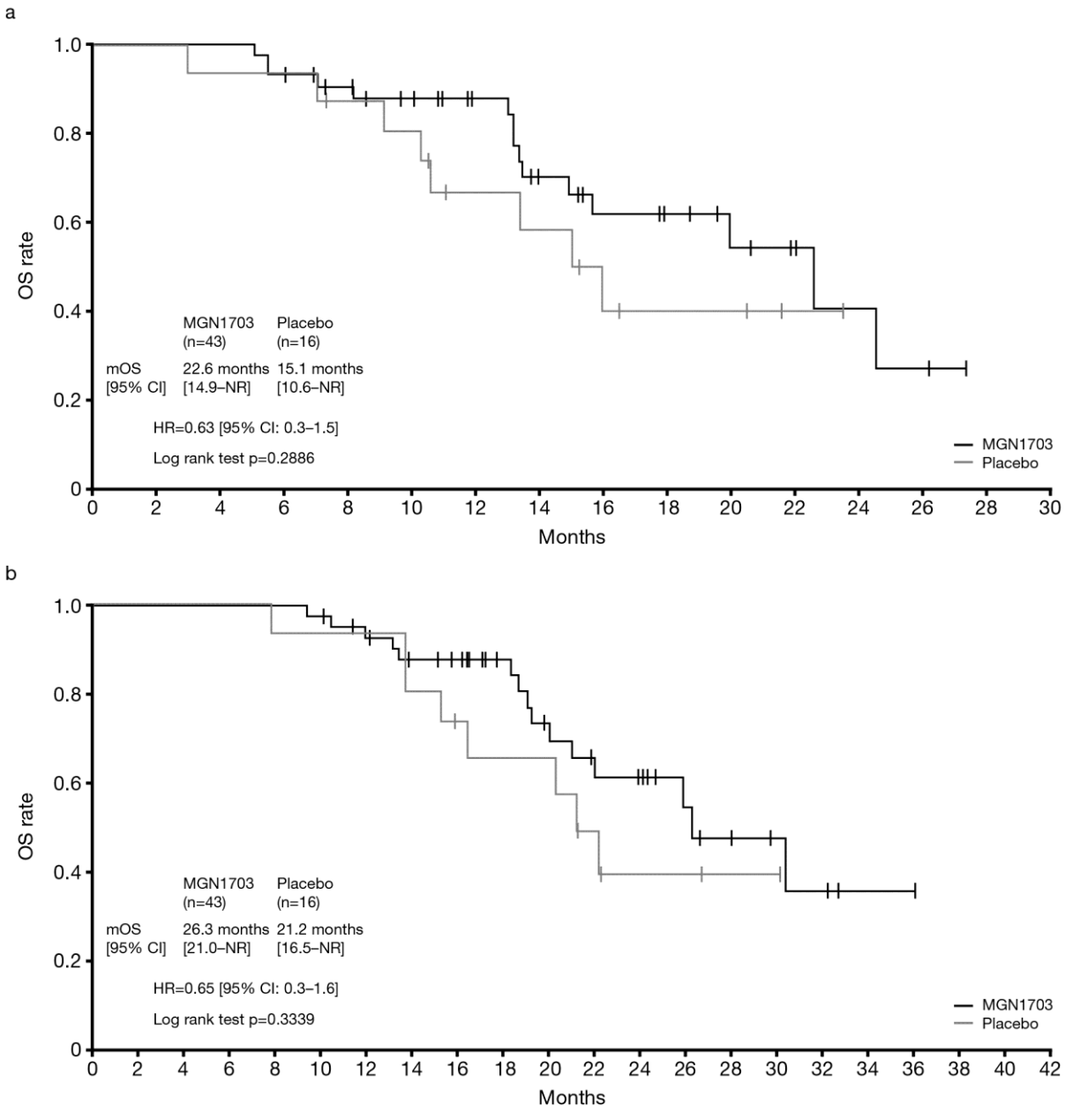
Web extra material (Appendix): overall survival

Fig. S1 OS by treatment group from (a) randomisation and (b) the start of induction therapy

Data are immature (>50% of patients are censored)

CI confidence interval; *HR* hazard ratio; *mOS* median overall survival; *NR* not reached; *OS* overall survival



Data are immature (>50% of patients are censored)

Web extra material (Appendix): protocol-defined exploratory analyses of baseline patient characteristics predictive for progression-free survival

Methodology

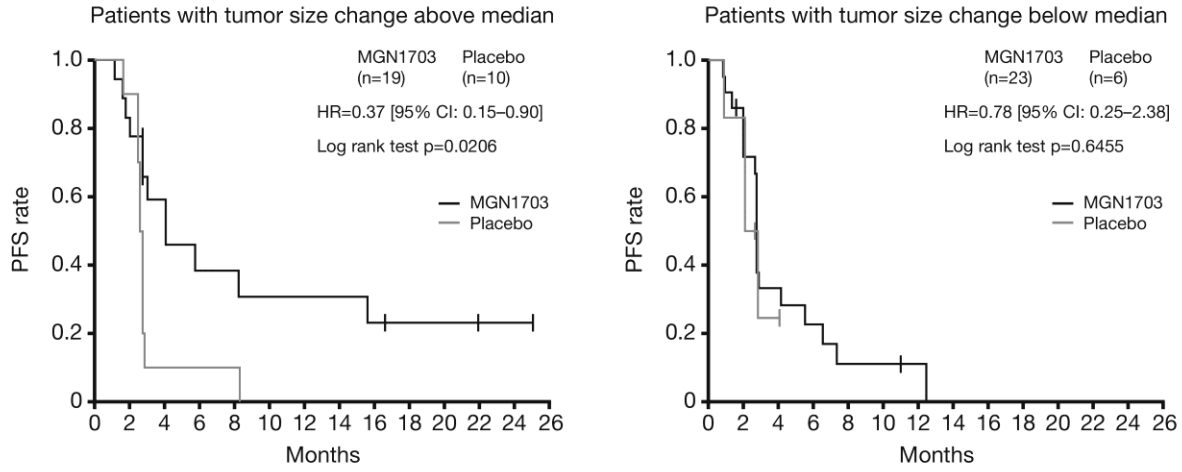
Baseline characteristics evaluated included age, gender, Eastern Cooperative Oncology Group performance status, resection of primary tumour, *KRAS* mutation status, type and duration of first-line chemotherapy, change in tumour size and best response (Response Evaluation Criteria in Solid Tumors) following first-line chemotherapy, and levels of carcinoembryonic antigen, alkaline phosphatase, lactate dehydrogenase, albumin, serum glutamic-oxaloacetic transaminase, thrombocytes and lymphocytes. Significant baseline prognostic factors (level of significance set at 0.10) were selected and entered a multivariate Cox proportional hazards model.

Results

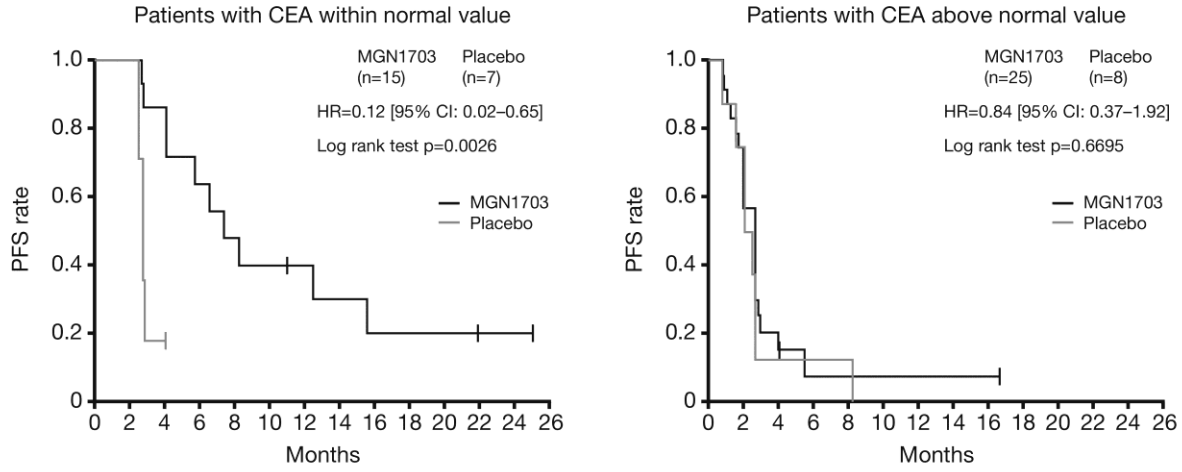
Fig. S2 Exploratory analysis of factors predictive of PFS

CEA carcinoembryonic antigen; *CI* confidence interval; *HR* hazard ratio; *PFS* progression-free survival; *SD* stable disease

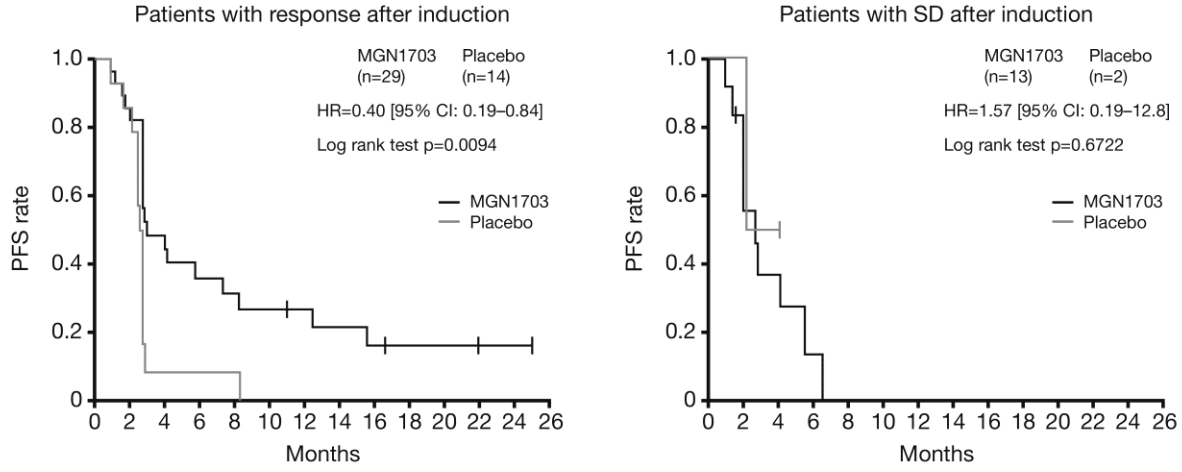
a Median change in tumour size following induction therapy



b Carcinoembryonic antigen concentrations following induction therapy



c Best response after induction therapy

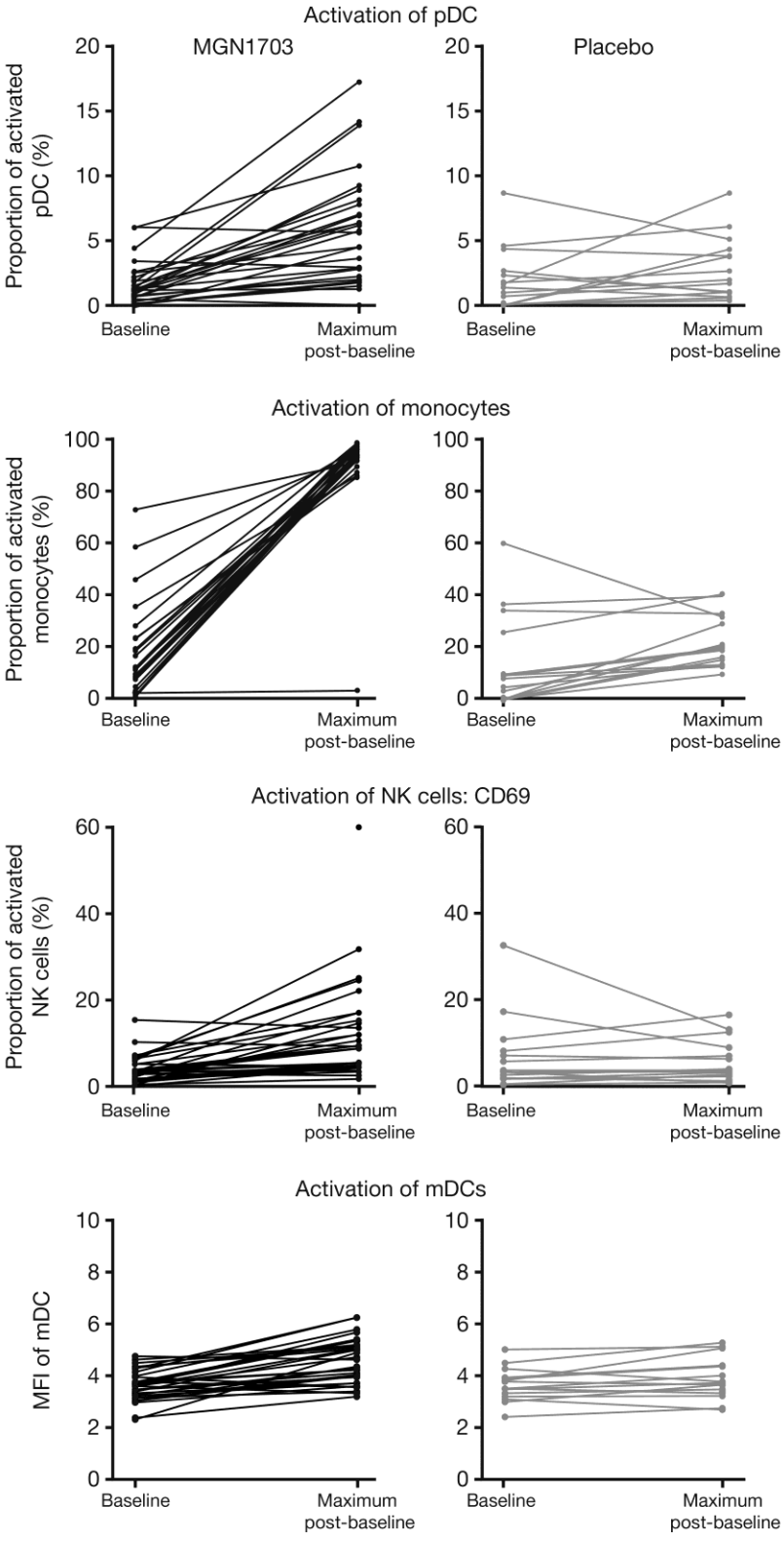


Web extra material (Appendix): immune system activation

Several cell populations (monocytes, B-lymphocytes, T-lymphocytes, NKT cells, NK cells, plasmacytoid dendritic cells and myeloid dendritic cells) were explored to evaluate the immunologic response to MGN1703. Monocytes and plasmacytoid dendritic cells were strongly activated, NK cells were activated and myeloid dendritic cells were not activated (Fig S3). NKT cells were activated, while T cells were slightly activated and B cells were not activated (figures not shown).

Fig. S3 Evidence for activation of the immune system by MGN1703 is shown by a treatment-induced increase in activated pDC in the total pDC population and the proportion of activated monocytes in the total monocyte population.

mDC myeloid dendritic cells*; MFI* mean fluorescence intensity value; *NK* natural killer cell; *pDC* plasmacytoid dendritic cell


Activation of pDC
MGN1703
Placebo
Proportion of activated pDC (%)
20
15
10
5
0
Baseline
Maximum post-baseline
Activation of monocytes
Proportion of activated monocytes (%)
100
80
60
40
20
0
Activation of NK cells: CD69
Proportion of activated NK cells (%)
60
40
20
0
Activation of mDCs
MFI of mDC
10
8
6
4
2
0