THE LANCET
Oncology

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Bromberg JEC, Issa S, Bakunika K, et al. Rituximab in patients with primary CNS lymphoma (HOVON 105/ALLG NHL 24): a randomised, open-label, phase 3 intergroup study. *Lancet Oncol* 2018; published online Jan 7. http://dx.doi.org/10.1016/S1470-2045(18)30747-2.

Supplement to:

Bromberg JEC, Issa S, Bakunina K et al. Role of Rituximab in Primary Central Nervous System Lymphoma Patients: Results of the Randomised Phase III HOVON 105 / ALLG NHL 24 Intergroup Study.

Table S1. Response by arm and age group:

	MBVP		R-MBVP	
	Age ≤ 60	Age >60	Age ≤ 60	Age >60
N	47	53	47	52
After (R-)MBVP				
CR/Cru	14 (30%)	22 (42%)	15 (32%)	15 (29%)
PR	29 (62%)	21 (40%)	28 (60%)	27 (52%)
ORR	43 (91%)	43(81%)	43 (91%)	42 (81%)
<PR	4 (8%)	10 (18%)	4 (8%)	10 (19%)
After HD Cytarabine				
CR/Cru	21 (45%)	32 (60%)	18 (38%)	27 (52%)
PR	18 (38%)	7 (13%)	24 (51%)	12 (23%)
ORR	39 (83%)	39 (74%)	42 (89%)	39 (75%)
<PR	8 (17%)	14 (27%)	5 (11%)	13 (25%)
End of treatment				
CR/Cru	34 (72%)	32 (60%)	40 (85%)	27 (52%)
PR	2 (4%)	7 (13%)	1 (2%)	12 (23%)
ORR	36 (77%)	39 (74%)	41 (87%)	39 (75%)
<PR	11 (24%)	14 (27%)	6 (13%)	13 (25%)

Table S2. treatment by arm and age group:

	MBVP			R-MBVP		
	ALL	Age ≤ 60	Age >60	ALL	Age ≤ 60	Age >60
R/R to start Rx* (d, IQR)	1 (1-3)†	1 (0-10)	1(0-10)	1 (1-4)	1(0-8)	1(0-11)
Cycle 1 MBVP (N) Day 1MTX Dose reduction n(%)	100 2 (2%)	47 0 (0%)	53 2 (4%)	99 2 (2%)	47 0 (0%)	52 2 (4%)
Cycle 1 MBVP (N) day 15 MTX dose reduction n(%) median delay (d, IQR)‡§	100 12 (12%) 1 (0-1)	47 3 (6%) 0 (0-1)	53 9 (17%) 0 (0-3)	99 13 (13%)% 1 (1-3)	47 4 (8%) 1 (1-2)	52 9 (18%) 1 (1-5)
Cycle 1 Rituximab (N) dose reduction n (%) rel dose intensity (IQR)	- -	- -	- -	99 20 (20%) 1.00 (0.92-1.01)	47 7 (15%)	52 13 (25%)
Cycle 2 MBVP (N) day 1 MTX dose reduction n (%) median delay (d, IQR)	92 6 (7%) 1 (0-6)	46 1 (2%) 1 (0-3)	46 5 (11%) 1 (0-7)	88 8 (9%) 1 (0-5)	43 3 (7%) 1 (0-4)	45 5 (11%) 2 (0-6)
Cycle 2 MBVP (N) day 15 MTX dose reduction n (%) median delay (d, IQR)	92 20 (22%) 0 (0-1)	46 8 (17%) 0 (0-0)	46 12 (26%) 0 (0-3)	88 16 (18%) 1 (1-2)	43 5 (12%) 1 (1-1)	45 11 (24%) 1 (1-3)
Cycle 2 Rituximab (N) dose reduction n (%) rel dose intensity (IQR)	- -	- -	- -	88 13 (15%) 0.91 (0.71-1.00)	43 5 (12%)	45 8 (18%)
Cytarabine (N) dose reduction n (%) median delay (d, IQR)	83 0 (0%) 4(0-9)	41 0 (0%) 3(0-7)	42 0 (0%) 5(0-10)	78 1 (1%) 6(1-10)	39 0 (0%) 6(1-9)	39 1 (3%) 4(1-12)
IT treatment, N (%)	8 (8%)	3 (6%)	5 (9%)	8 (8%)	4 (9%)	4 (8%)
WBRT given (N)	34	34	-	36	36	-

boost N (%)	15 (44%)	15 (44%)	-	24 (67%)	24 (67%)	-

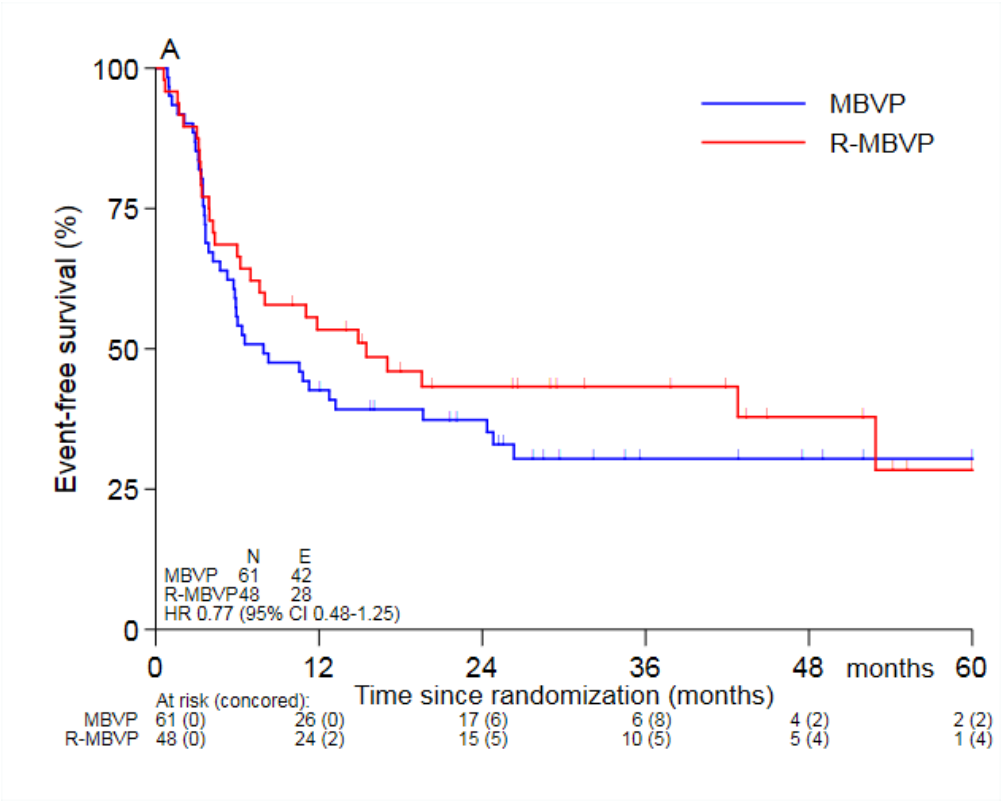
R/R = date of registration and randomisation
*= time between simultaneous registration/randomization and initiation of treatment in days
†after exclusion of single outlier of 40 days;
‡ Only day 15 MTX in cycle 1 was more frequently delayed in older patients in arm B but median differed by only 1 day (14 vs 15)
§Presentation of delays is restricted to patients who have received the respective treatment.
IQR = inter-quartile range

Table S3. Supportive care: administration of G-CSF, platelet and red blood cell transfusions

Cycle	MBVP arm	R-MBVP arm	Total
Cycle 1 (R)-MBVP			
G-CSF given n (%)	17 (17%)	20 (20%)	37 (19%)
No of PLT transfusions, median (IQR)	0 (0-0)	0 (0-0)	0 (0-0)
No of RBC transfusions, median (IQR)	0 (0-0)	0 (0-0)	0 (0-0)
Cycle 2 (R)-MBVP			
G-CSF given n(%)	21 (23%)	15 (17%)	36 (20%)
No of PLT transfusions median (IQR)	0 (0-0)	0 (0-0)	0 (0-0)
No of RBC transfusions, median (IQR)	0 (0-2)	0 (0-2)	0 (0-2)
HD-Ara-C			
G-CSF given n(%)	17 (20%)	16 (21%)	33 (20%)
No of PLT transfusions median (IQR)	1 (0-1)	1 (0-1)	1 (0-1)
No of RBC transfusions, median (IQR)	0 (0-1)	0 (0-1)	0 (0-1)

PLT=platelet; RBC = red blood cell; IQR = inter-quartile range

Figure S1: EFS by arm and sex. A: male; B: female



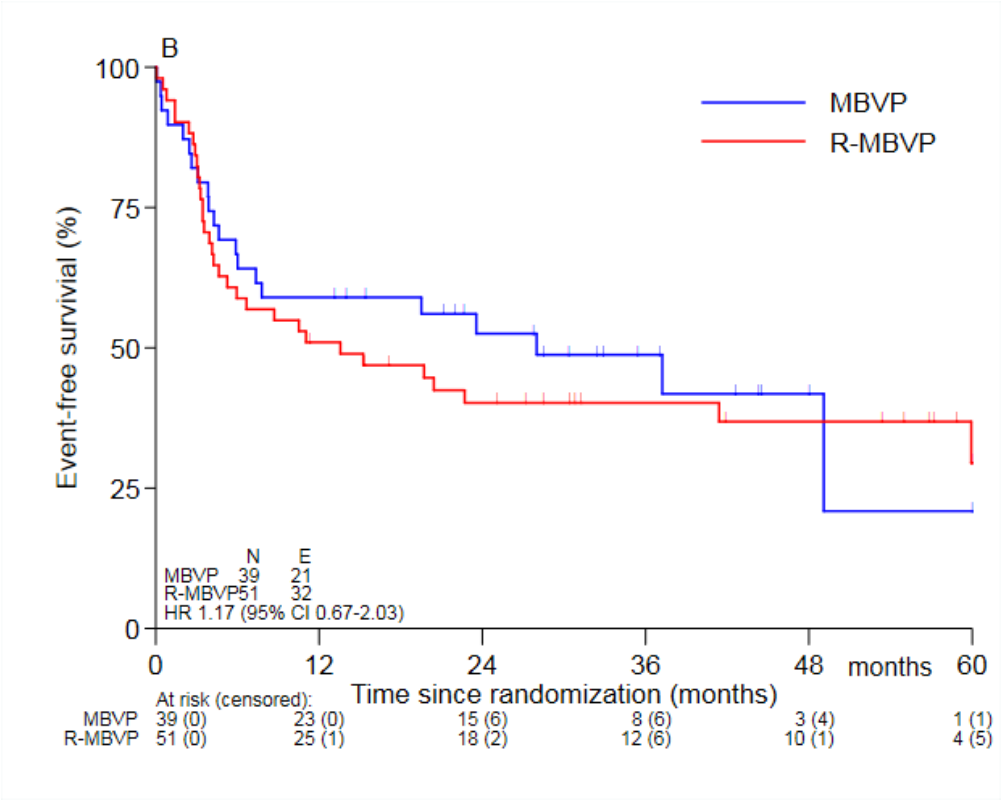


Figure S2-A. Neutrophil recovery after first cycleMBVP

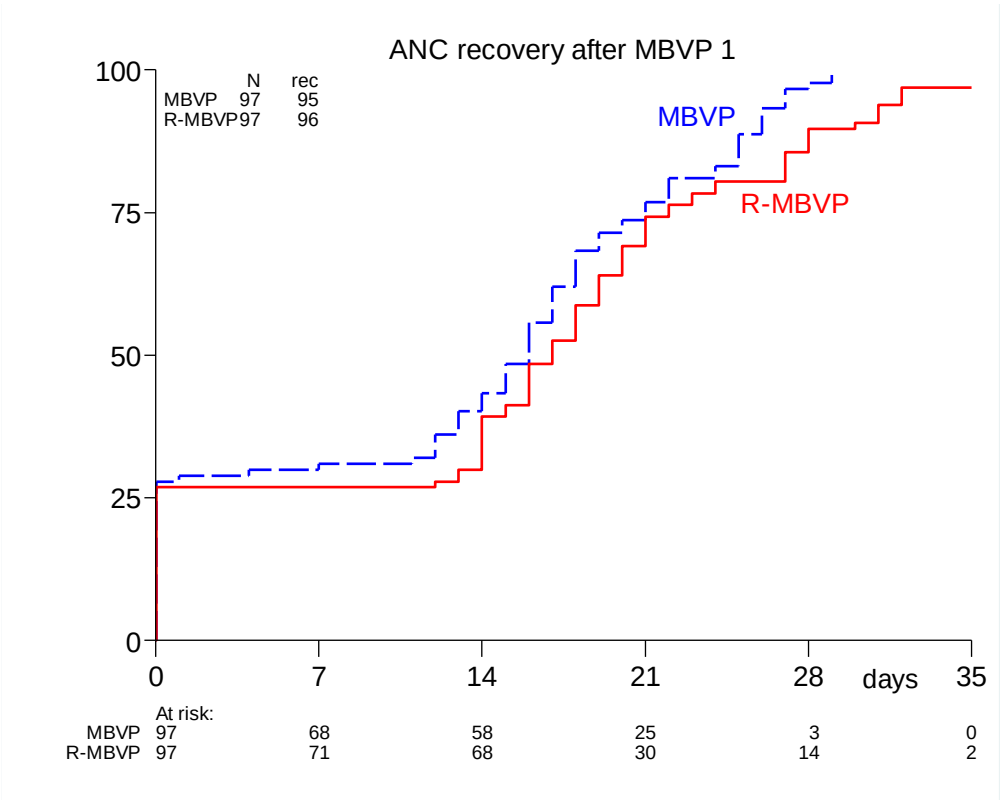


Figure S2-B. Neutrophil recovery after second cycleMBVP

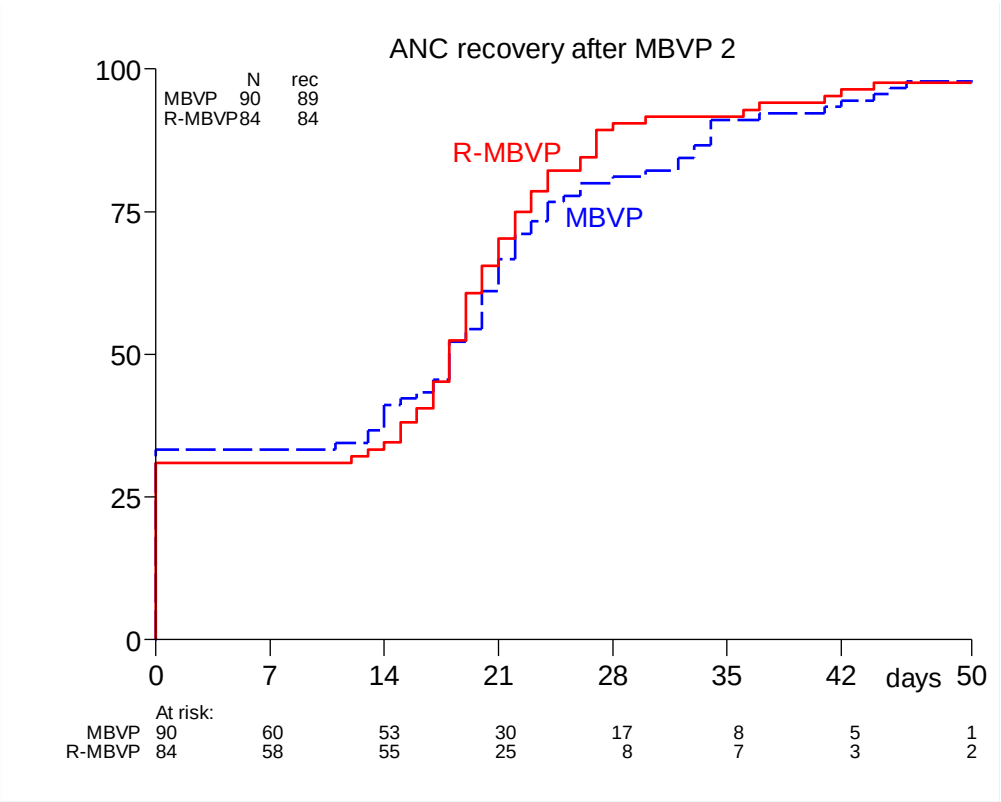


Figure S3-A. Platelet recovery after first cycle MBVP

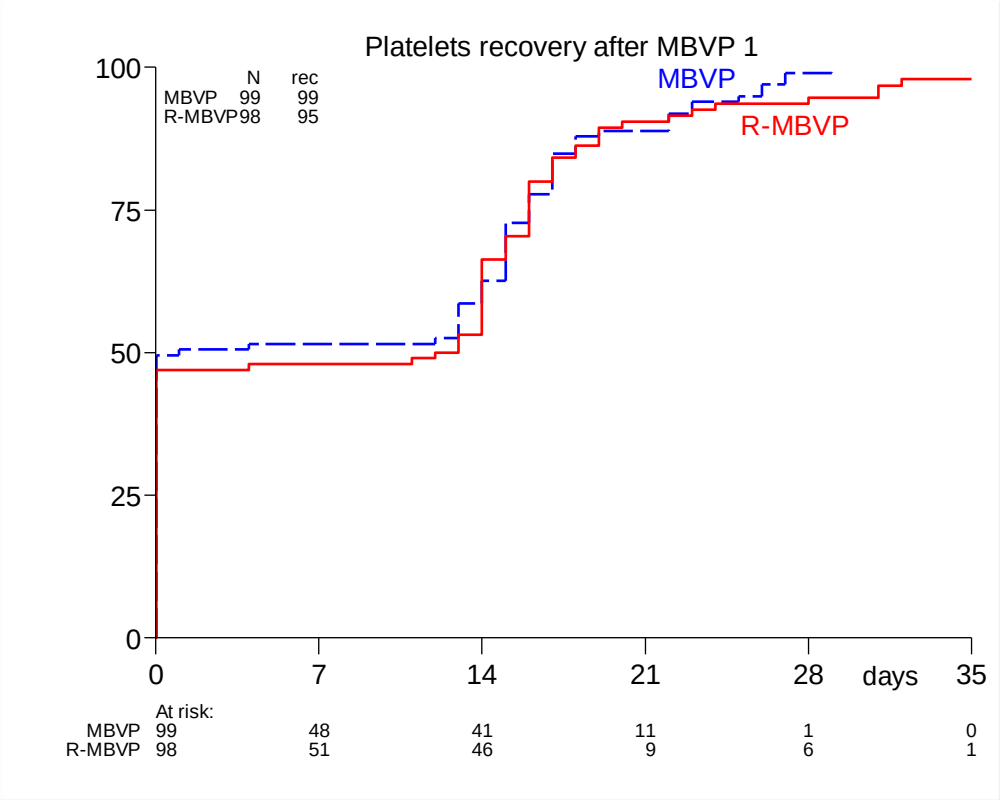
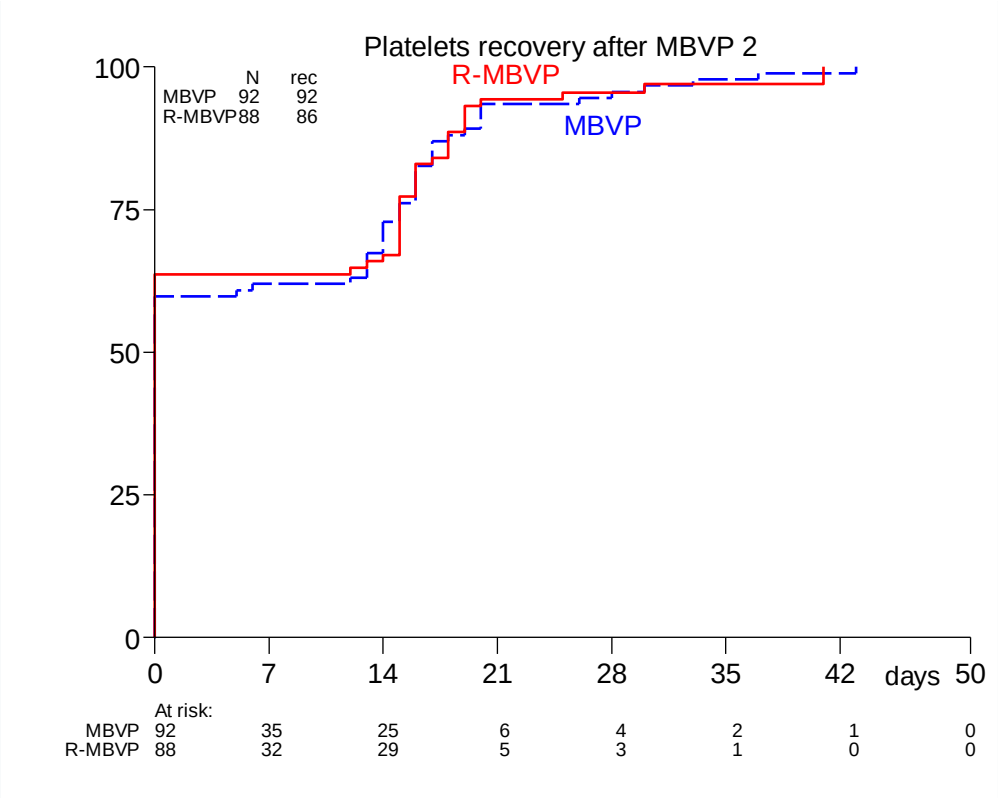


Figure S3-B. Platelet recovery after second cycle MBVP



Contributing sites, local principle investigators, and number of patients included per site

Erasmus MC Cancer Institute, Rotterdam, The Netherlands; J.K. Doorduijn MD	51
University Medical Center Utrecht, The Netherlands; M.C. Minnema MD	23
ETZ Hospital, Tilburg, The Netherlands; M. Durian MD	17
Middlemore Hospital, Auckland, New Zealand; S. Issa MD	15
Sir Charles Gairdner Hospital, Nedlands, Australia; G. Cull MD	10
Radboud University Medical Center, Nijmegen, The Netherlands; W.B.C. Stevens MD	9
University Medical Center, Maastricht, The Netherlands; H.C. Schouten MD	8
VU Medical Center, Amsterdam, The Netherlands; J.M. Zijlstra MD	8
Spaarne Gasthuis, Haarlem, The Netherlands; A. Beeker MD	7
University Medical Centre Groningen, The Netherlands; M. Nijland MD	7
Netherlands Cancer Institute, Amsterdam, The Netherlands; J.W. Baars MD	7
Royal Melbourne Hospital, Melbourne, Australia; K.D. Mason MD	7
Haga Hospital, Den Haag, The Netherlands; L.H. Bohmer MD	6
Antonius Hospital, Nieuwegein, The Netherlands; O. de Weert MD	5
Royal Adelaide Hospital, Adelaide, Australia; P. Giri MD	5
Martini Hospital, Groningen, The Netherlands; A.W.G. van der Velden MD	3
Isala Hospital, Zwolle, The Netherlands; M. van Marwijk Kooy MD	3
Princess Alexanddra Hospital, Brisbane, Australia; S. Mapp MD	3
Royal Hobart Hospital, Hobart, Australia; A. Johnston MD	1
Concord Hospital, Concord, Australia; J. Estell MD	1
Jeroen Bosch Hospital, Den Bosch, The Netherlands; J.F.M. Pruit MD	1
Medisch Spectrum Twente, Enschede, The Netherlands; M.R. Schaafsma MD	1
Royal Prince Alfred Hospital, Camperdown, Australia; S. Larsen MD	1

HOVON 105/ALLG NHL 24 Data Sharing Statement

Individual participant data collected for this study including a data dictionary defining each field in the concerned dataset will be made available for other research to others upon request, after approval by the HOVON executive board.

De-identified participant data including a data dictionary will be made available, as well as the study protocol and statistical analysis plan, if relevant for the study question.

The data will be available immediately after publication until a maximum of 15 years after the study has ended.

Data sharing proposals should be directed to HOVON by completing a Data Request Form which can be retrieved from www.hovon.nl. The proposal will be considered by the HOVON Executive Board, who will consult the Principle Investigator(s) and relevant Working Group members. The requested data will be accessible after the proposal has been approved.
Criteria for data sharing are defined in the HOVON Data Confidentiality Policy which can be publically consulted on the HOVON website.