Maintenance Rituxan is associated with improved clinical outcome in Rituxan naïve patients with Waldenstrom's Macroglobulinemia who respond to a Rituxan containing regimen.

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Introduction

Rituxan

- A monoclonal antibody.
- Active agent in the treatment of Waldenstrom's Macroglobulinemia.
- Chimeric anti CD 20 antibody.
- Originally used in monotherapy.
- Rituxan vigorously pursued because of non-myelosuppressive nature and potential to synergize with various agents.

Introduction

•With the use of single agent Rituxan, ORR of 20-30% and PFS of 1 year is observed with standard induction regimen.

•The use of extended Rituxan schedule ORR of 40-50% and PFS of 16-30 months is reported.

• In combination therapy, higher ORR (70-90%) and PFS (3-4 years) have been observed.

Introduction

- Despite all this success most pts with WM still progress
- MRx has increasingly become used and studied of potential benefit
- Efficacy and safety must be investigated in WM patients

Study Design

- Identification of all Rituxan naïve patients treated at our center with the diagnosis of WM who received Rituxan containing induction therapy.
- The primary endpoints : determination of best categorical response attainment, progression free survival (PFS), overall survival (OS), and safety among patients observed versus those who received MRX.
- Changes in immunoglobulin level and blood counts following MRx were also assessed for both groups.

Baseline Characteristics

	Patients on Observation	Patients who received MR	p-value
N=	162	86	NA
Age (years)	61	62	0.755
Previously Untreated	117 (72.2%)	64 (74.4%)	0.710
BM Involvement (%)	40	50	0.068
Serum IgM	3695	3640	0.844
Serum IgA	42	49	0.455
Serum IgG	493	553	0.656
Hematocrit (%)	31.0	33.0	0.155
Platelet Count ($x10^9L$)	213	162	0.419
Serum β_2M	3.3	2.8	0.626
Induction Therapy	56 (34.6%)	23 (26.7%)	0.265
Rituximab alone	106 (65.4%)	63 (73.3%)	0.265
Combination Therapy with Rituximab			

**Median # of induction infusions = 6 / Median # of MRx infusions= 8*

Categorical Responses Post-Induction			
CR	10 (6.2%)	3 (3.5%)	0.549
VGPR	12 (7.4%)	5 (5.8%)	0.841
PR	99 (61.1%)	52 (60.5%)	1.000
MR	39 (24.1%)	24 (27.9%)	0.610

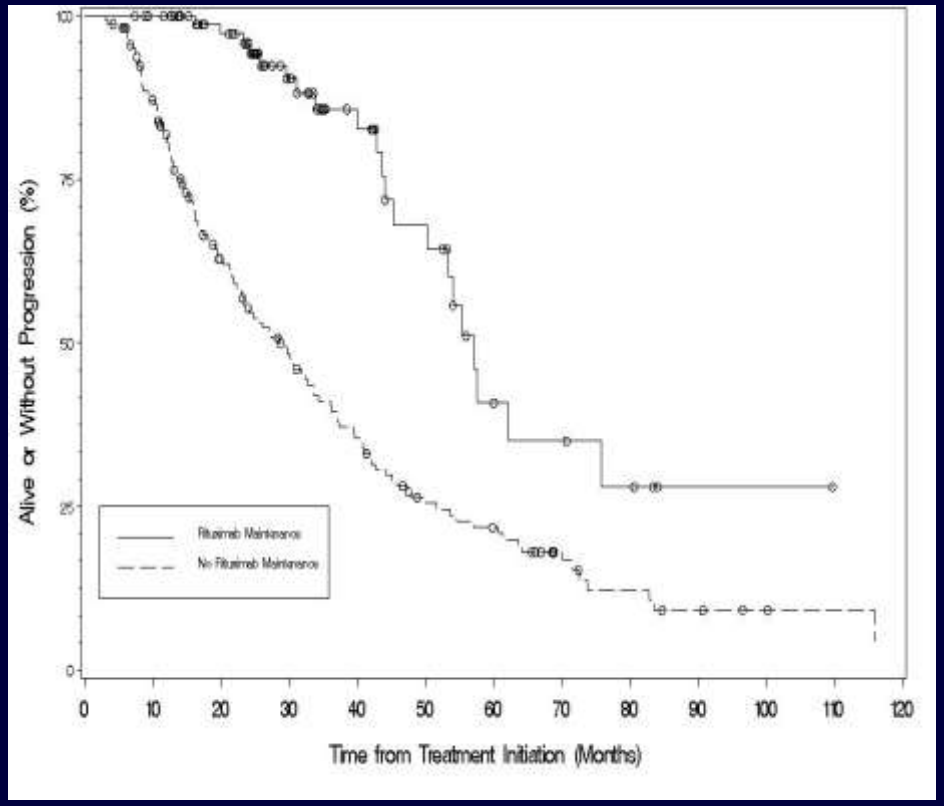
**Baseline Characteristics did not differ between both groups*

Baseline Characteristics

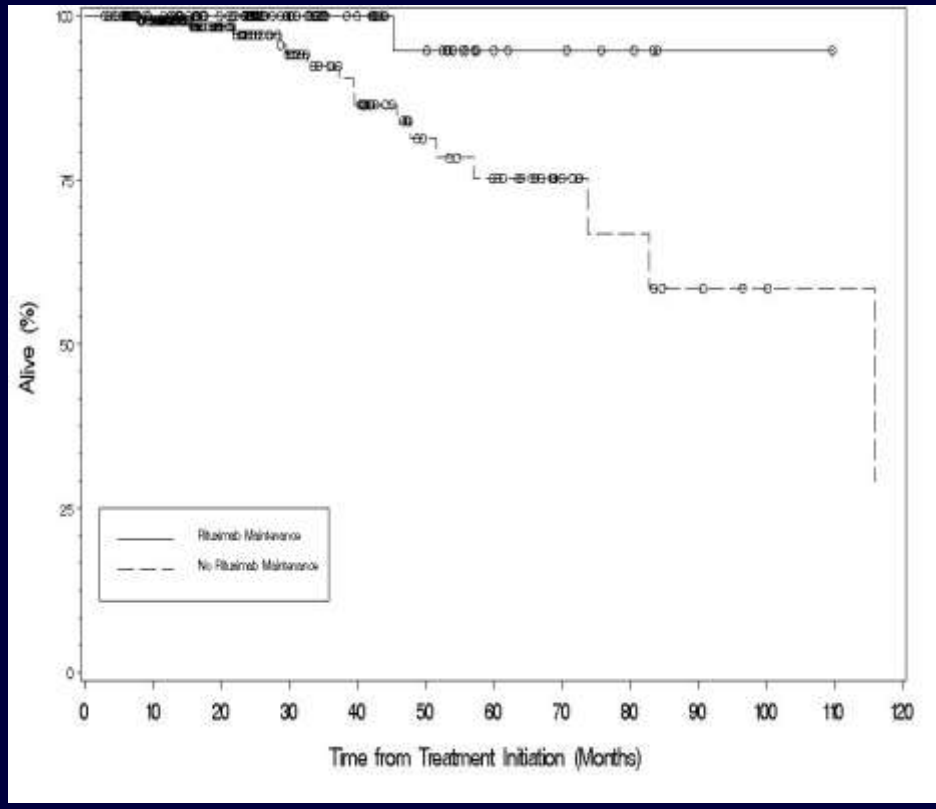
- 181 patients (73%) were previously untreated
- Induction Therapy included:
  - Rituxan monotherapy (79 patients)
  - Combination with Velcade (40 patients)
  - Combination with Cyclophosphamide (44 patients)
  - Combination with Immunomodulator Agent (31 patients)
  - Combination with Nucleoside Analogue(54 patients)

Progression free survival (A) and Overall survival (B) for 248 Rituxan naïve WM patients who underwent observation or maintenance Rituxan therapy.

A



B

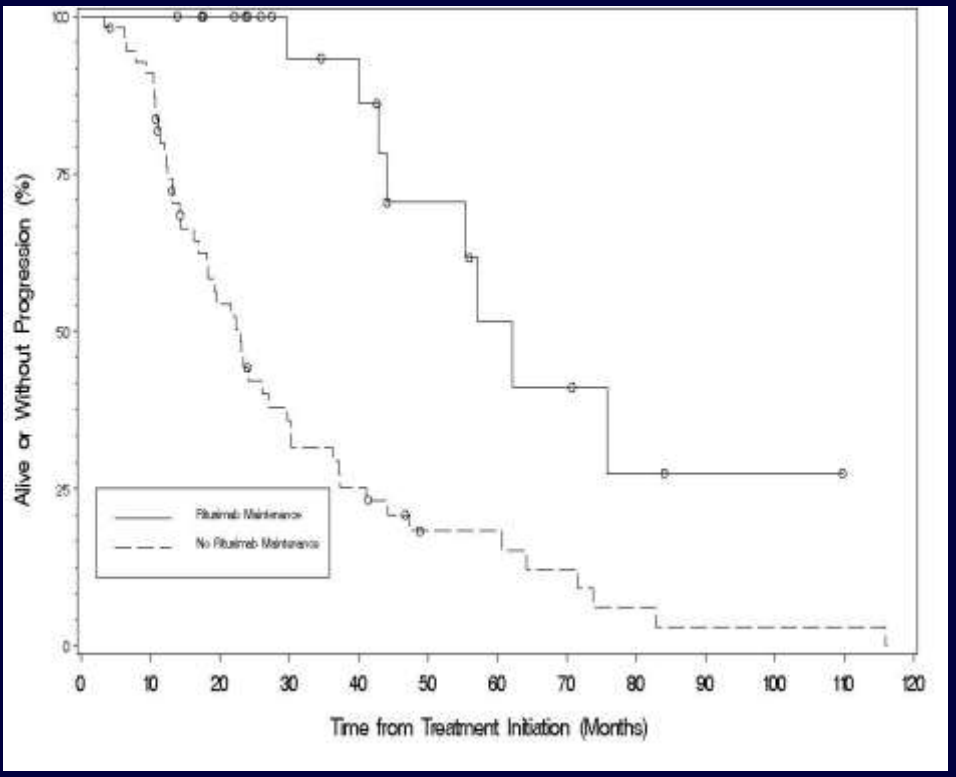


	Observation	Maintenance	p=
Median PFS	28.6 months	56.3 months	0.0001

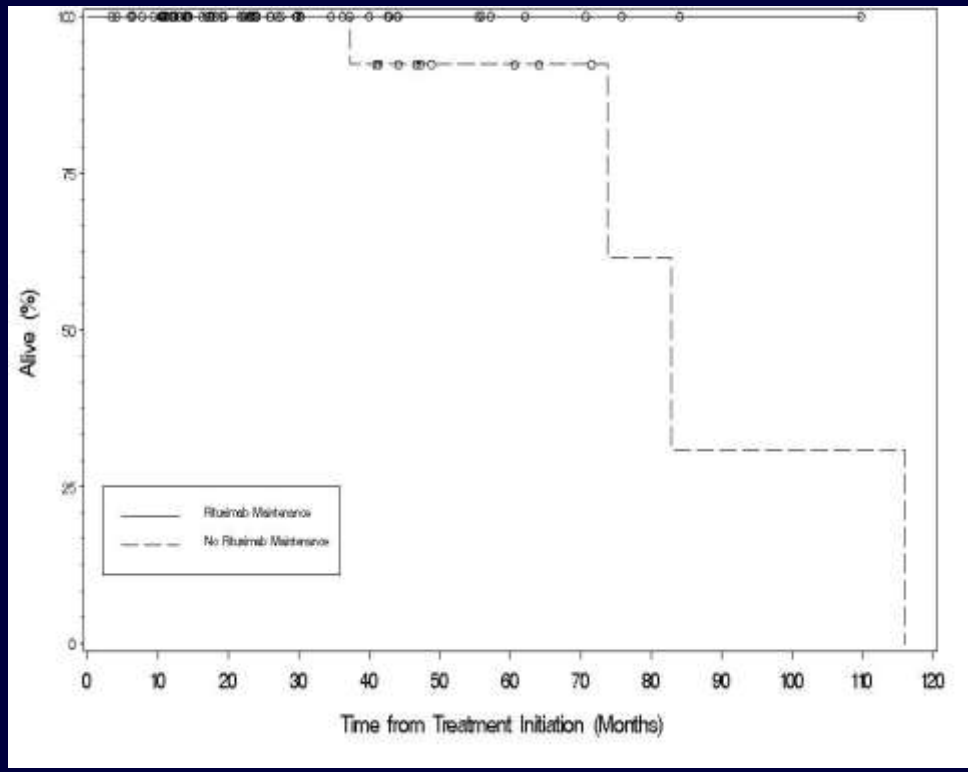
	Observation	Maintenance	p=
Median OS	116 months	>120 months	0.0095

Progression free survival (A) and Overall survival (B) for 79 Rituxan naïve WM patients who underwent observation or maintenance Rituxan therapy after Rituxan monotherapy.

A



B

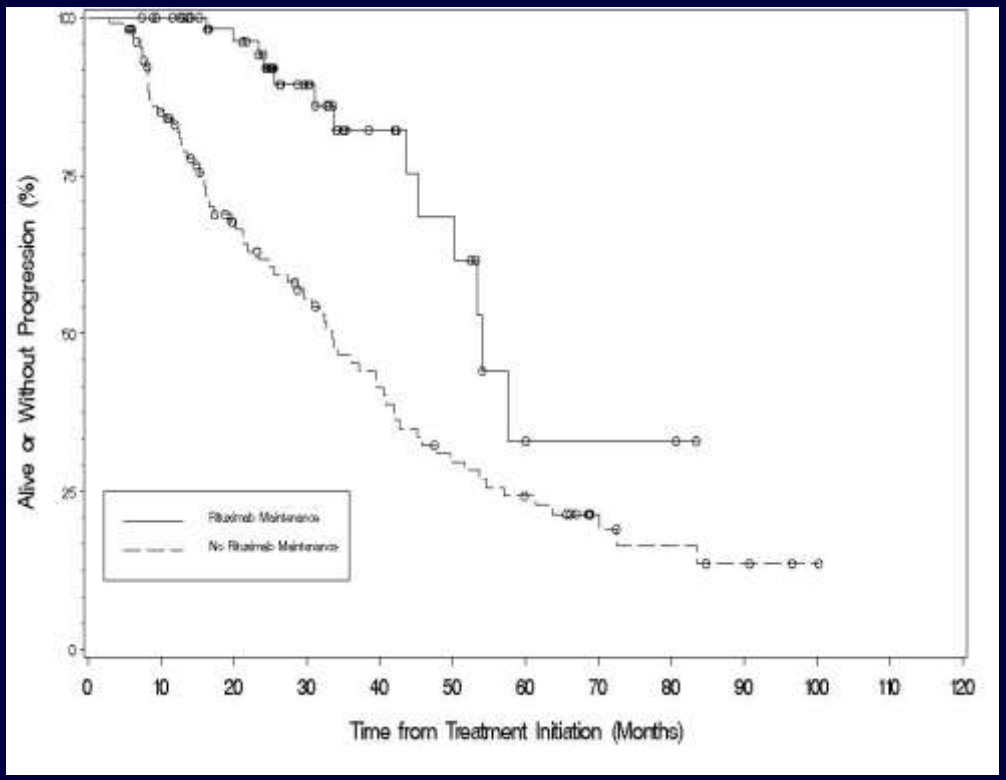


	Observation	Maintenance	p=
Median PFS	22.6 months	61.3 months	0.0001

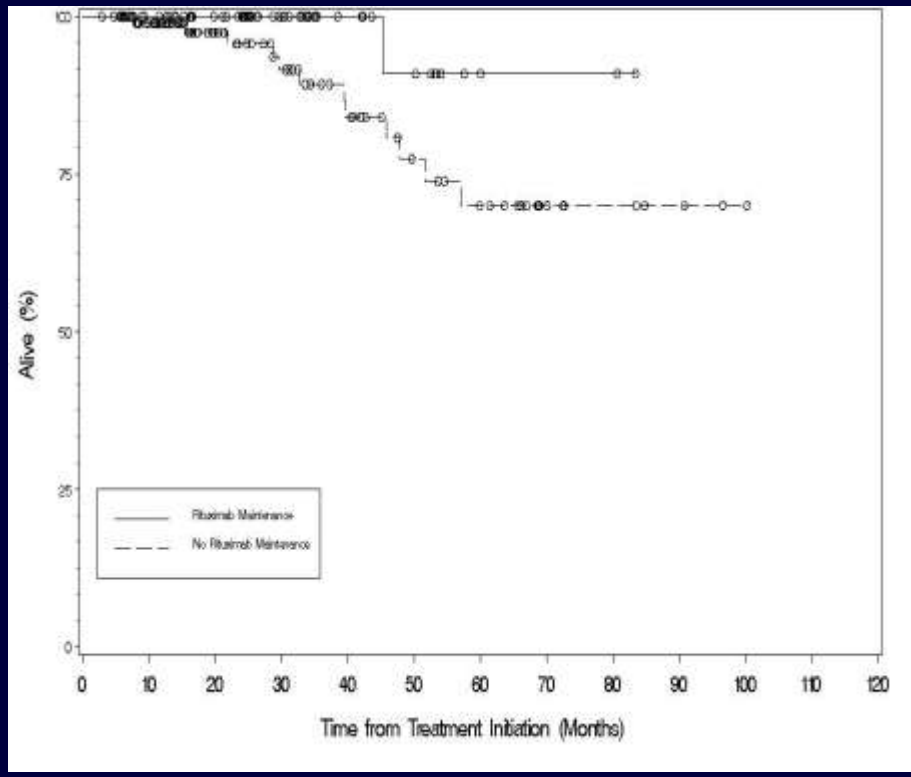
	Observation	Maintenance	p=
Median OS	82.9 months	>115 months	0.0833

Progression free survival (A) and Overall survival (B) for 169 Rituxan naïve WM patients who underwent observation or maintenance Rituxan therapy after Rituxan combination therapy.

A



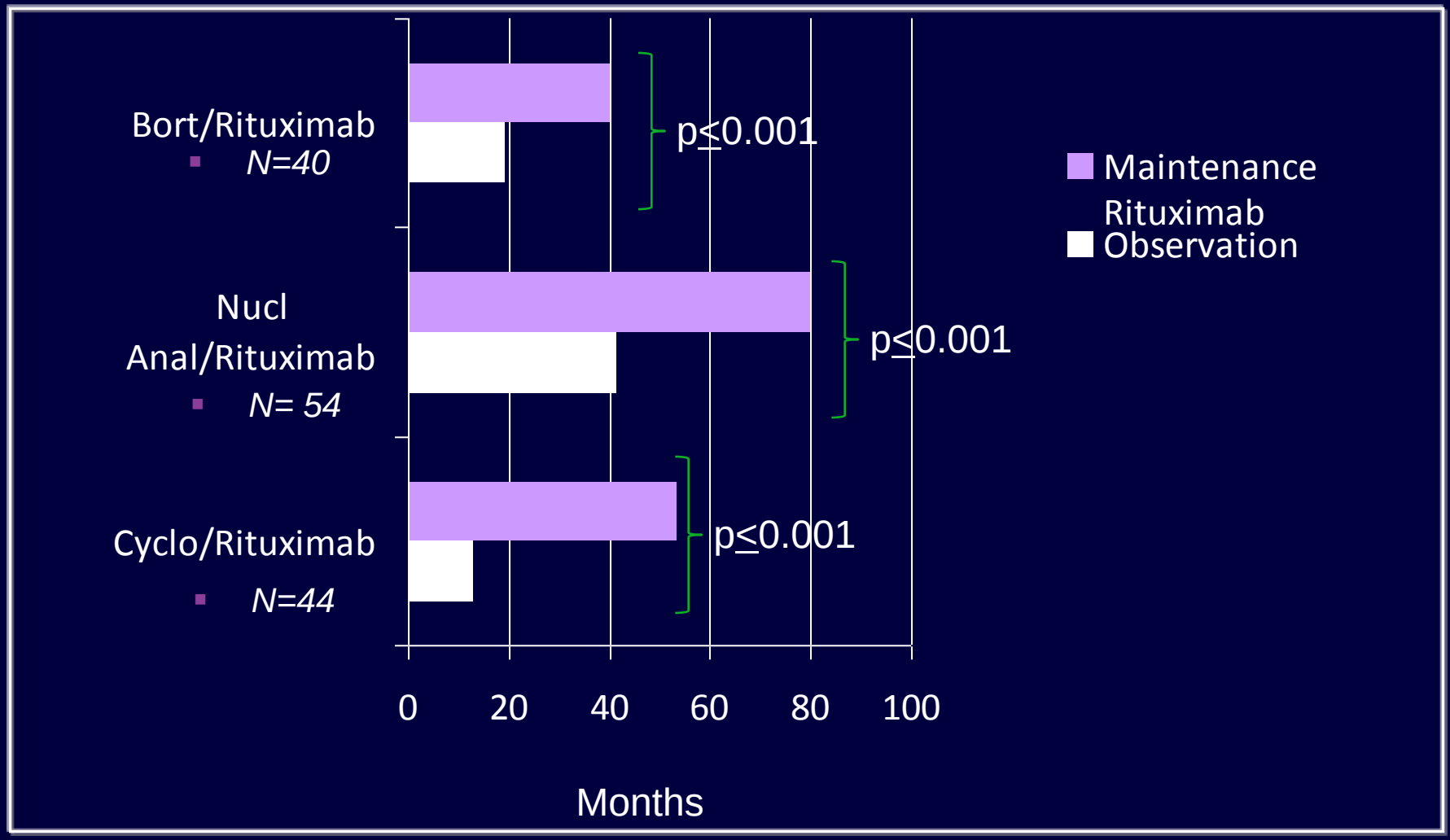
B



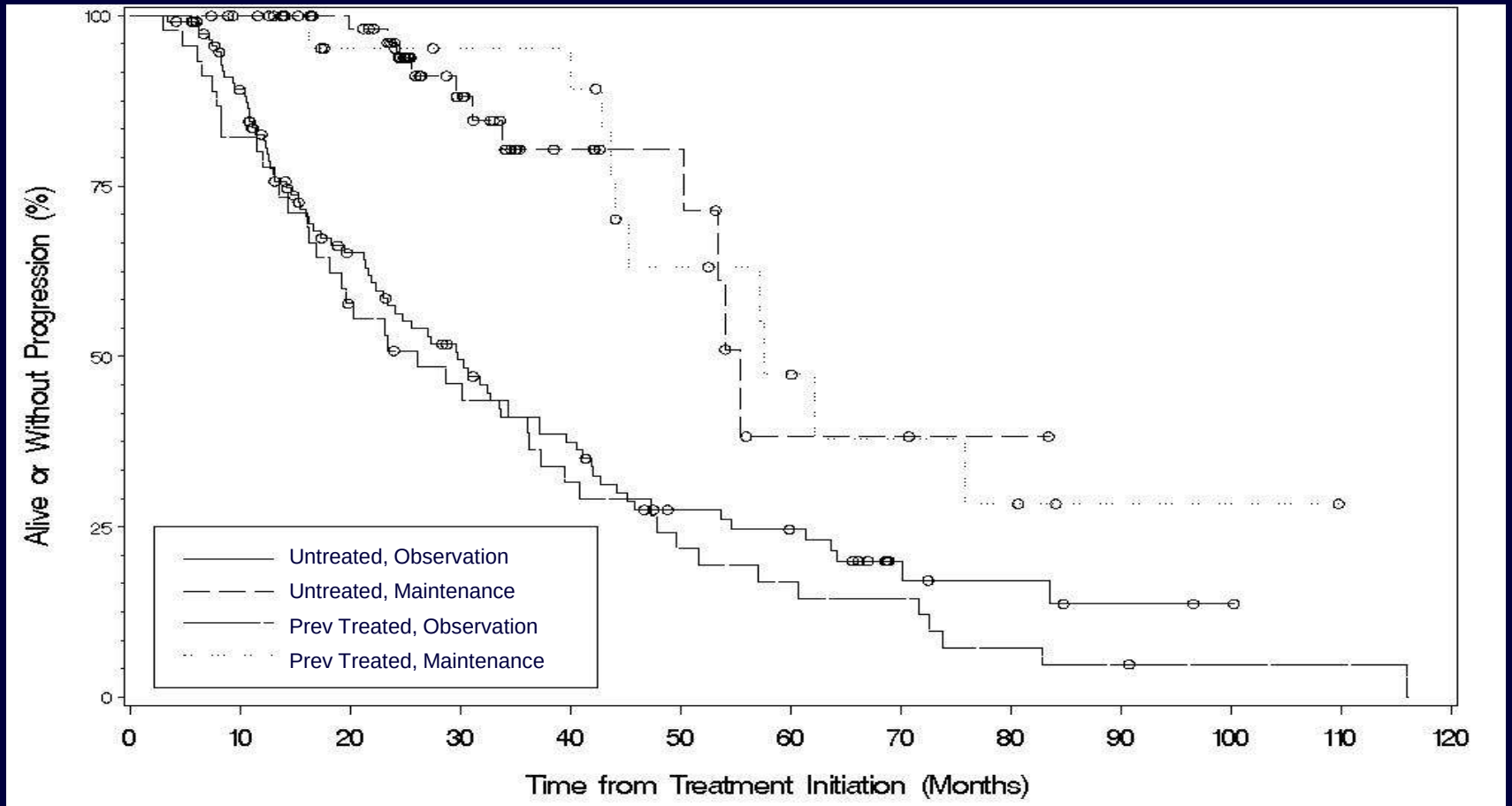
	Observation	Maintenance	p=
Median PFS	33.0 months	53.3 months	0.0001

	Observation	Maintenance	p=
Median OS	>80 months	>120 months	0.0410

Progression free survival stratified by treatment subgroup for Rituxan naïve WM patients who underwent observation or maintenance Rituxan therapy.

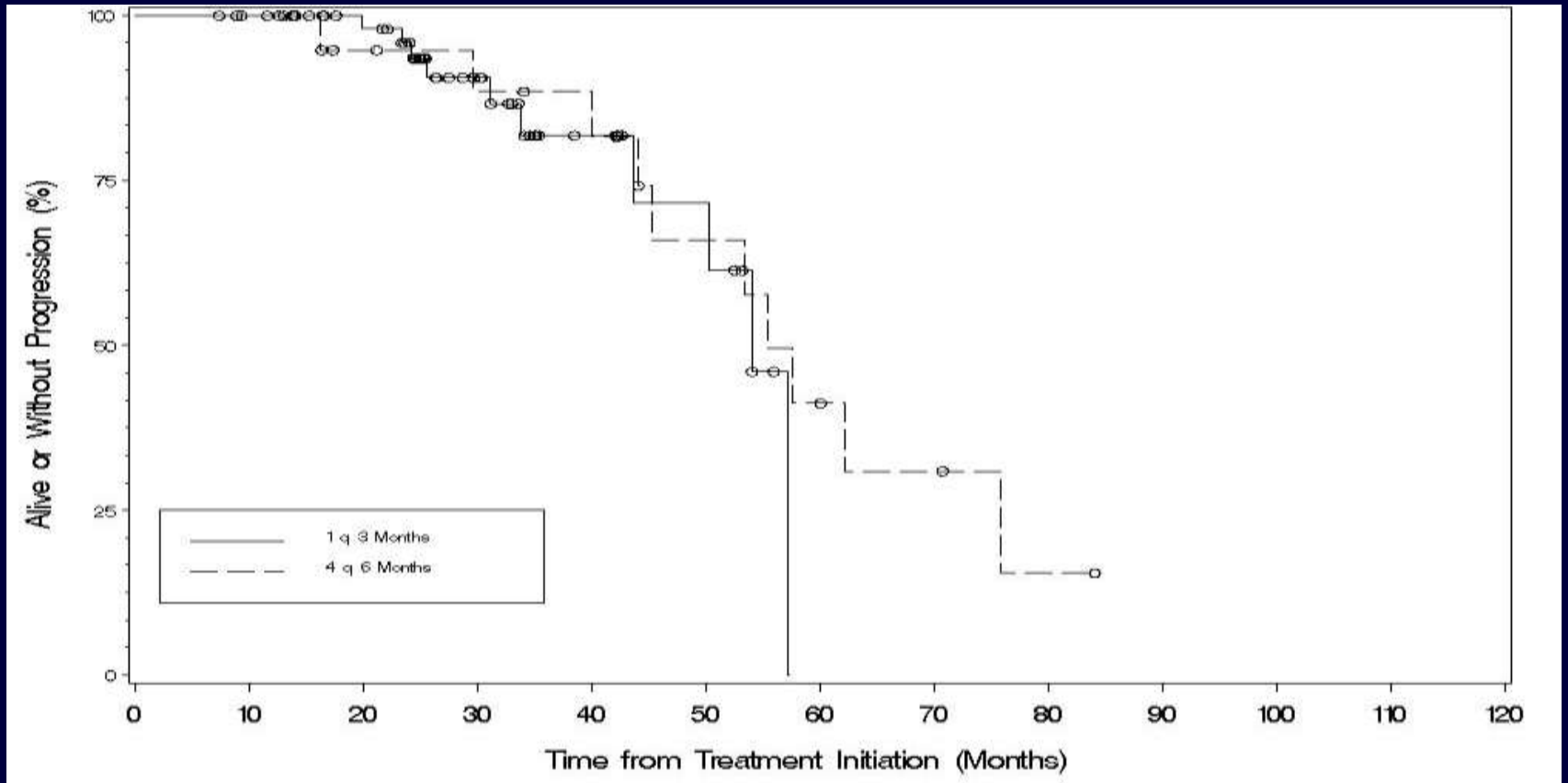


PFS stratified by previous treatment status for 248 Rituxan naïve WM patients who underwent observation or maintenance Rituxan therapy.



	Observation	Maintenance	p=
Untreated (Median PFS)	29.6 months	54.6 months	0.0001
Prev Treated (Median PFS)	25.6 months	56.7 months	0.0001

PFS for 86 Rituxan naïve WM patients who underwent maintenance therapy using either 4 weekly infusions q 6 months or 1 infusion q 3 months.

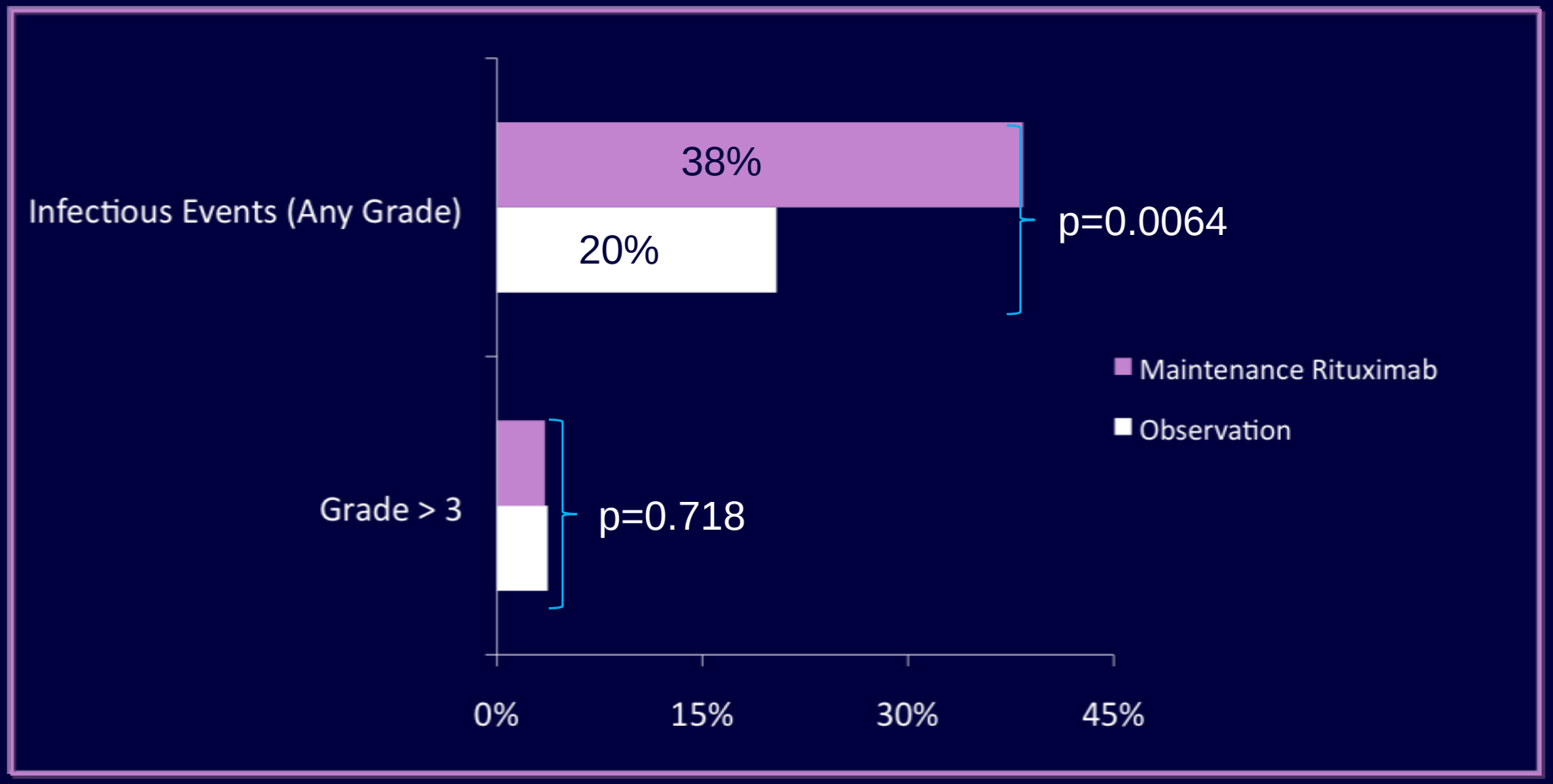


	1 q 3 months	4 q 6 months	p=
Median PFS	53.3 months	61.3 months	0.4921

Reported adverse events for 248 Rituxan naïve patients

	Patients on Observation	Patients who received MR	p-value
N=	162	86	
Arthralgias	1 (0.6%)	1 (1.2%)	0.773
Bronchitis	11 (6.8%)	8 (9.3%)	0.646
Encephalitis	1 (0.6%)	0 (0%)	0.751
Pneumonia	6 (3.7%)	5 (5.8%)	0.654
Headaches	1 (0.6%)	1 (0.1%)	0.773
Herpes Zoster	2 (1.2%)	3 (3.5%)	0.466
Hypersensitivity	5 (3.1%)	4 (4.7%)	0.462
Neutropenia, with fever.	2 (1.2%)	1 (1.2%)	0.577
Neutropenia, without fever.	1 (0.6%)	1 (1.2%)	0.773
Sinusitis	12 (7.4%)	13 (15.1%)	0.089
Skin Infection	1 (0.6%)	1 (1.2%)	0.773
Syncope	0 (0%)	1 (0.6%)	0.751
Upper Respiratory Tract Infection (NOS)	4 (2.5%)	6 (7.0%)	0.168

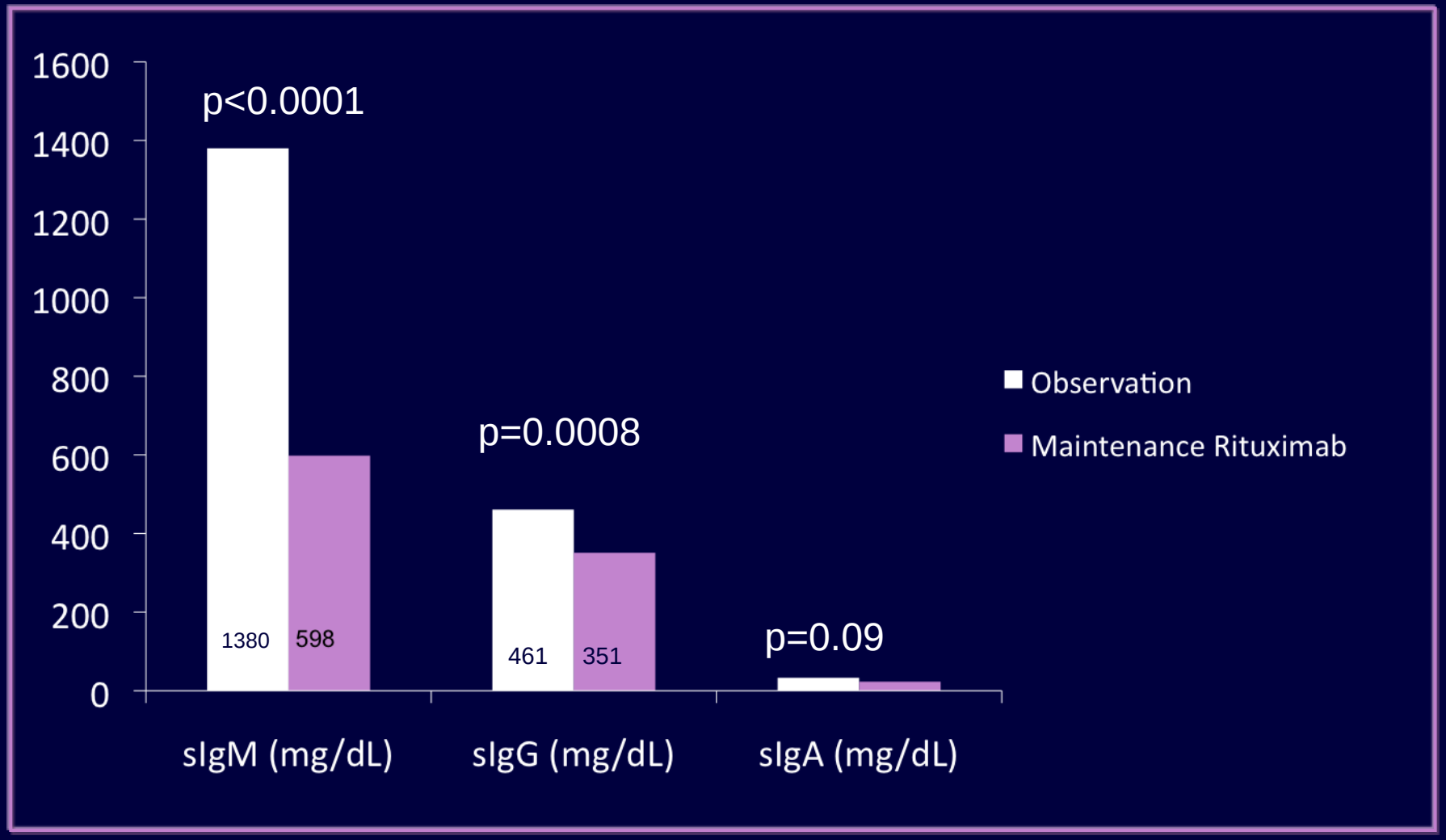
Infectious Events in WM patients Who Underwent Observation vs Maintenance Rituxan Therapy.



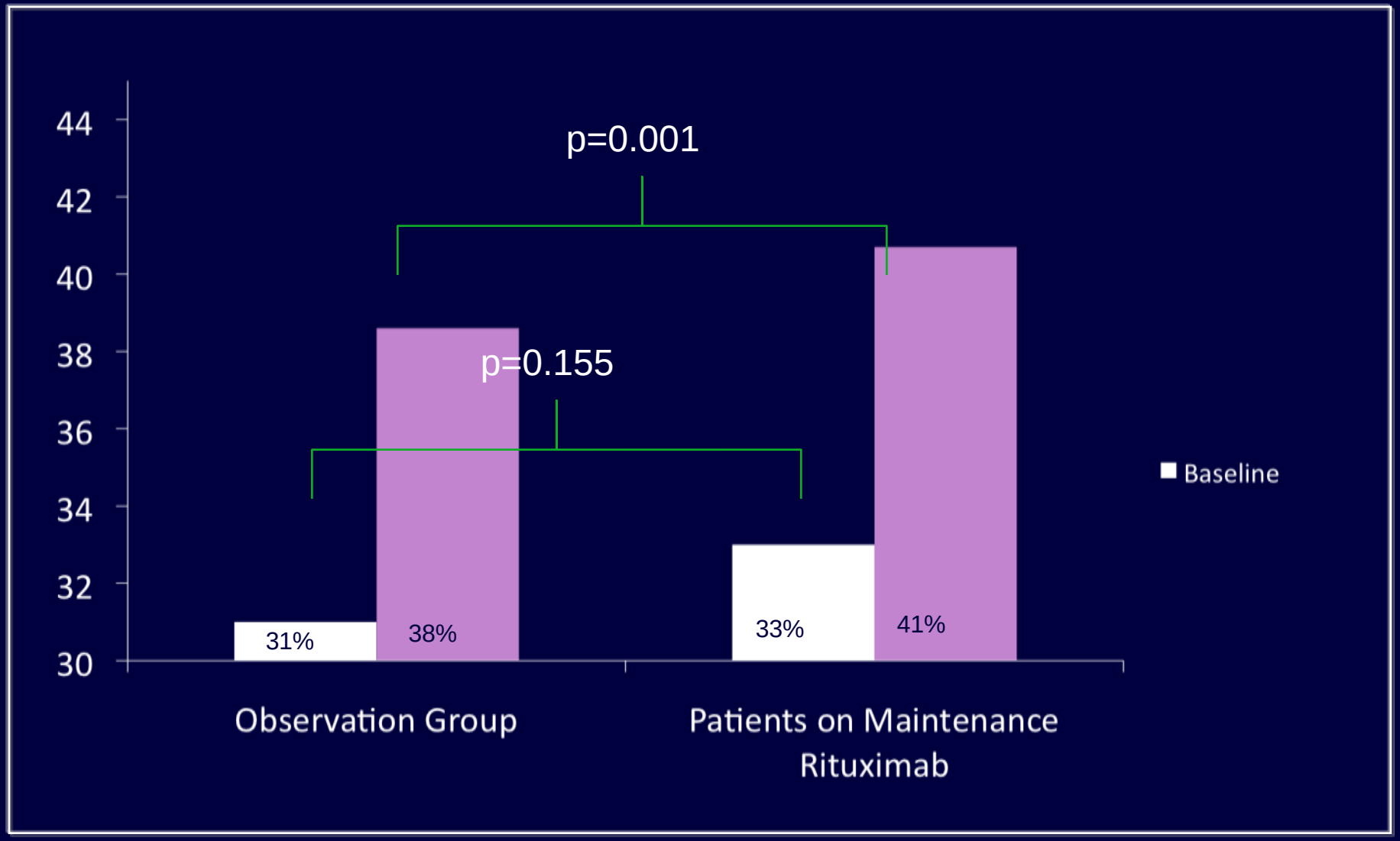
***Most Infectious Events involved the respiratory tract**

*** Nearly all these infections were grade 2 or less**

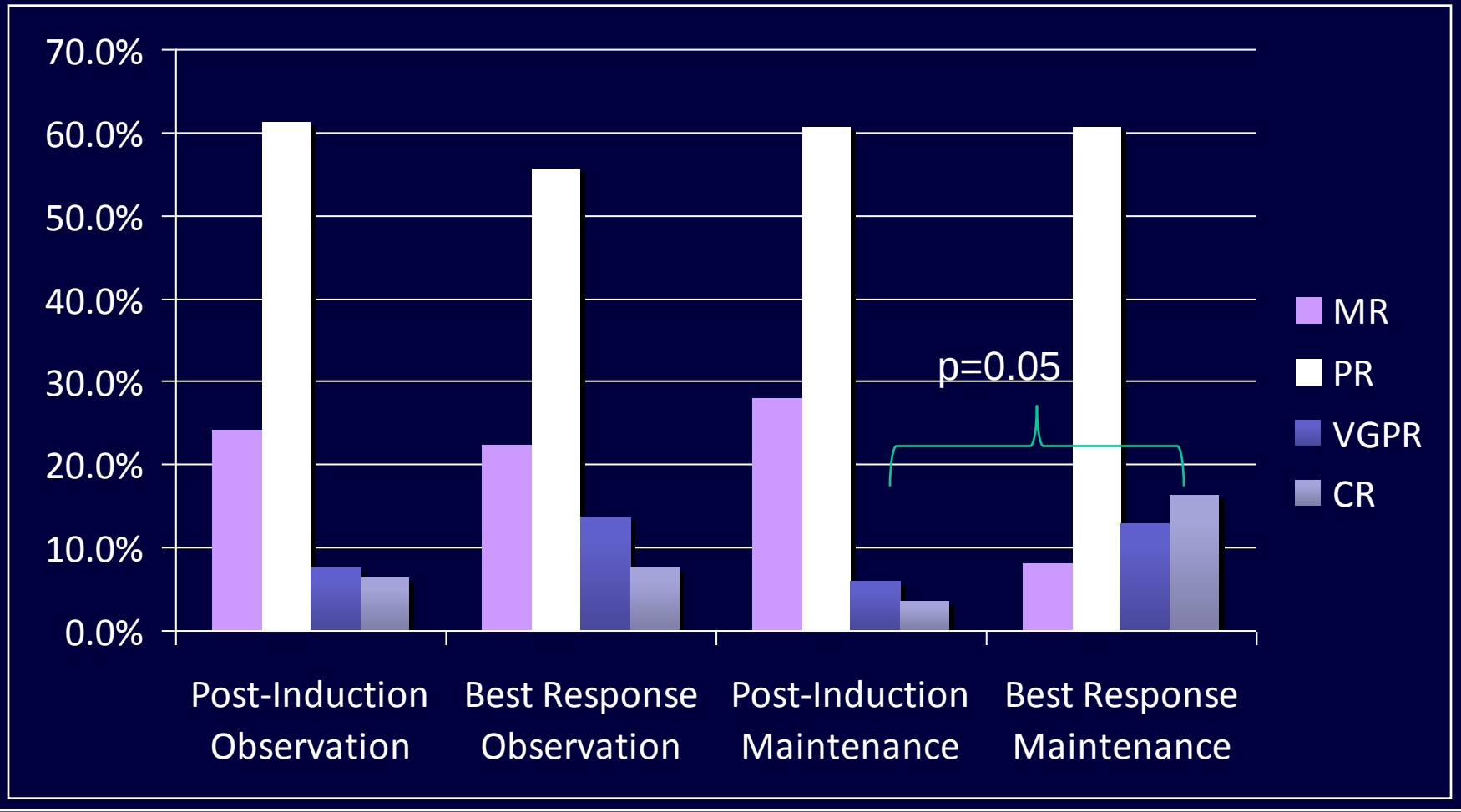
Impact of Maintenance Rituxan Therapy on Lowest Attained Serum Immunoglobulin Levels during Follow-up.



Impact of Maintenance Rituxan Therapy on Best Hematocrit Response During Follow-up.



Categorical response improvements in WM patients on observation versus maintenance Rituxan therapy.



**During post-induction follow-up, upgrade in categorical response occurred in 16/162 (10%) of patients on observation versus 36/86 (41.8%) of patients who received maintenance Rituxan (p<0.0001).

Questions to still be answered

- Ideal Schedule
- Duration of Maintenance Rituxan
- Benefit of Maintenance Rituxan over re-treatment

Summary

- The use of maintenance Rituxan in WM patients responding to a Rituxan containing regimen is associated with improved categorical responses, as well as prolonged progression free and overall survival.
- The benefit for maintenance Rituxan was observed in WM patients receiving Rituxan as monotherapy as well as combination therapy, and was independent of previous treatment status.
- Among patients receiving maintenance Rituxan, an increased number of infectious events were observed, though were mainly $\leq$ grade 2.


Center for Waldenström's Macroglobulinemia