ADVAGRAF™
tacrolimus prolonged release

Prograf™
tacrolimus

De novo Advagraf® vs Prograf® in Kidney Transplant Recipients

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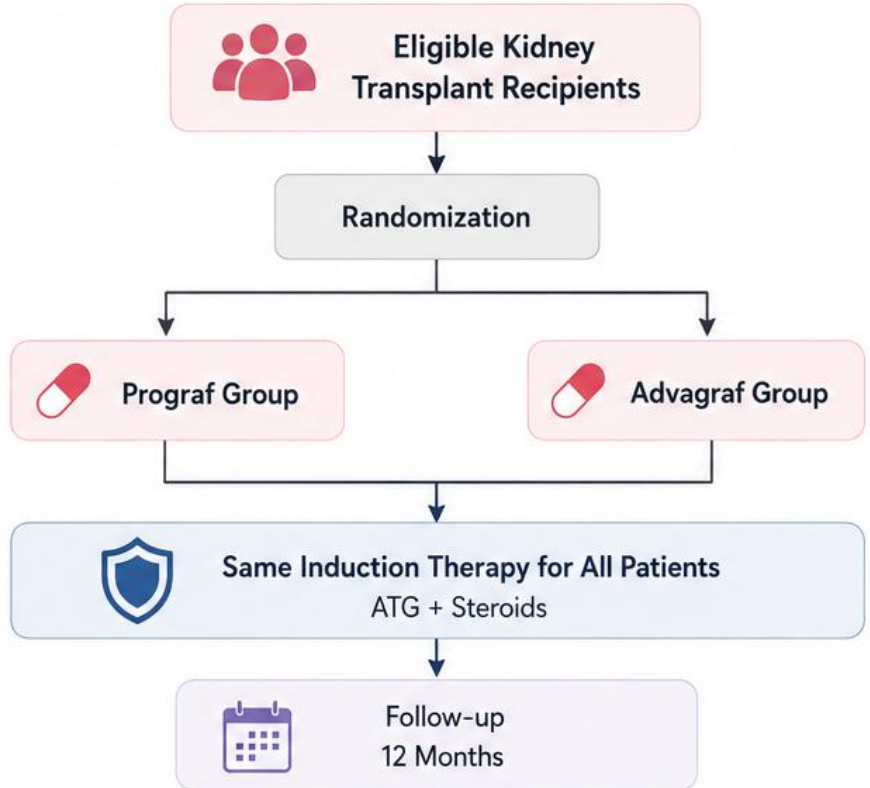
Efficacy, Safety and Adherence of Advagraf vs. Prograf in Kidney Transplant Recipients: A Randomized Clinical Trial

Study Design and Methods

- Single-center randomized clinical trial
- Kidney transplant recipients
- Labbafinejad Hospital, Tehran, Iran
- Follow-up duration: 12 months
- Same induction therapy in both groups



Objectives

- To compare efficacy between Advagraf and Prograf
- To compare safety between Advagraf and Prograf
- To compare adherence between Advagraf and Prograf

Outcomes Assessed

Efficacy

- Acute rejection
- Graft function (Serum Creatinine, eGFR)
- Graft survival

Safety

- BK virus infection
- Post-transplant diabetes
- De novo DSA

Adherence

- Intra-patient variability (IPV)
- Coefficient of variation (CV)

This randomized clinical trial aims to provide real-world evidence on the comparative effectiveness, safety, and adherence of Advagraf vs. Prograf over a 12-month follow-up.

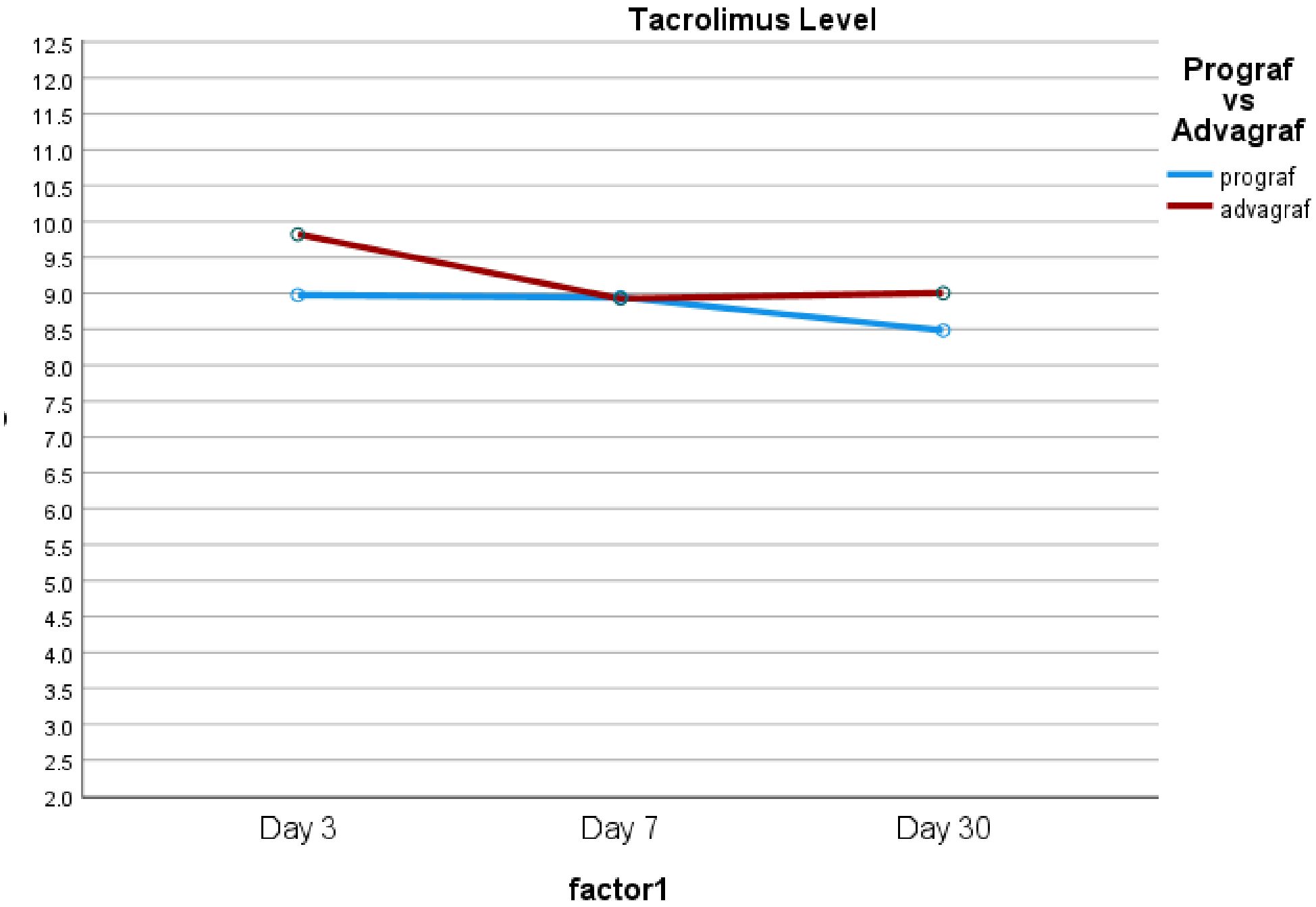
Labbafinejad Hospital
Tehran, Iran

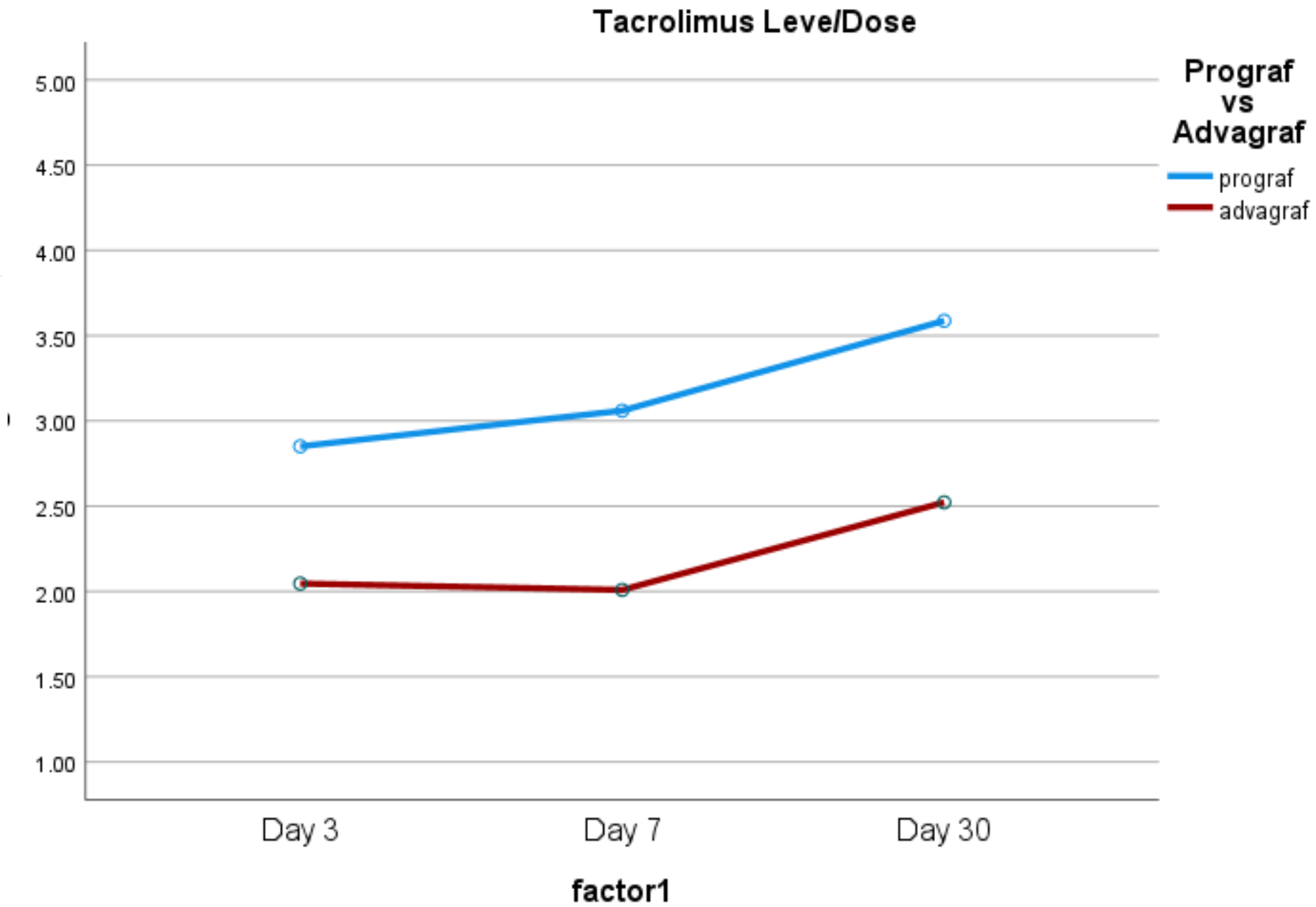
Demographic Data

Variable	Prograf	Advagraf	P-Value
Total Patient	203	111	
Male: Female	136 : 67 (67% : 33%)	68 : 43 (61.3% : 38.7%)	0.324
Mean Age (years)	44±16	45±15	0.548
Living : Deceased	136 : 67 (67% : 33%)	72 : 39 (64.9% : 35.1%)	0.710

First Month Drug Level

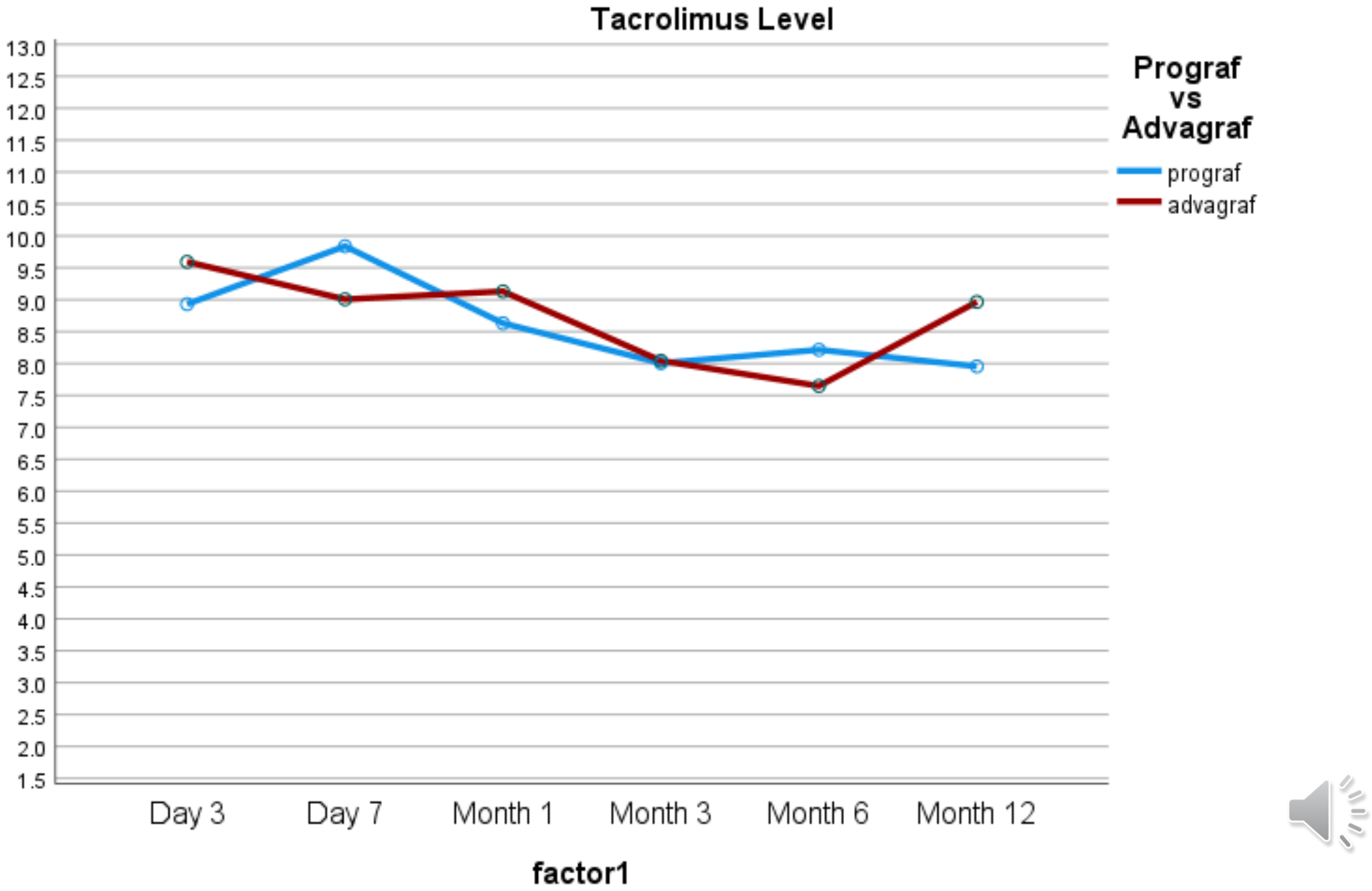
Variable	Prograf	Advagraf	P-Value
First Dose (mg/kg)	0.073 ± 0.027	0.074 ± 0.026	0.856
C_0 Day 3	9.4 ± 5.6	10.1 ± 5.2	0.325
C_0/Dose Day 3	2.75 ± 3.3	2.1 ± 1.3	0.783
C_0 Day 7	9.5 ± 4.2	9.3 ± 4.5	0.512
C_0/Dose Day7	3 ± 3.1	1.9 ± 1.1	**0.003**
C_0 month 1	8.7 ± 3.3	8.9 ± 3.7	0.885
C_0/Dose Month 1	3.2 ± 4	2.4 ± 1.9	**0.047**

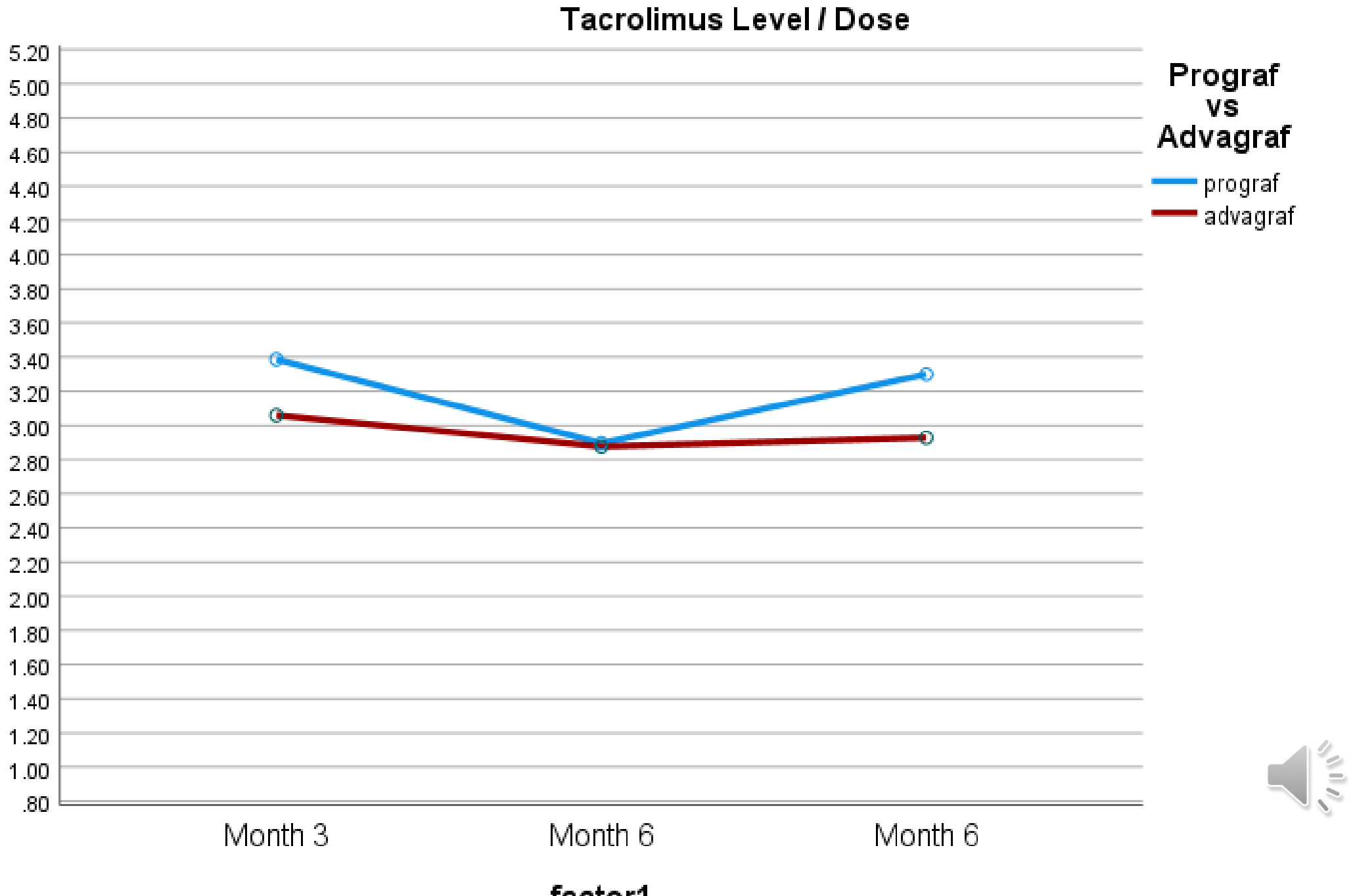

Tacrolimus Level
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
Day 3
Day 7
Day 30
factor1
Prograf vs Advagraf
prograf
advagraf


Tacrolimus Leve/Dose
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
Day 3
Day 7
Day 30
factor1
Prograf vs Advagraf
prograf
advagraf

12-Month Follow-up

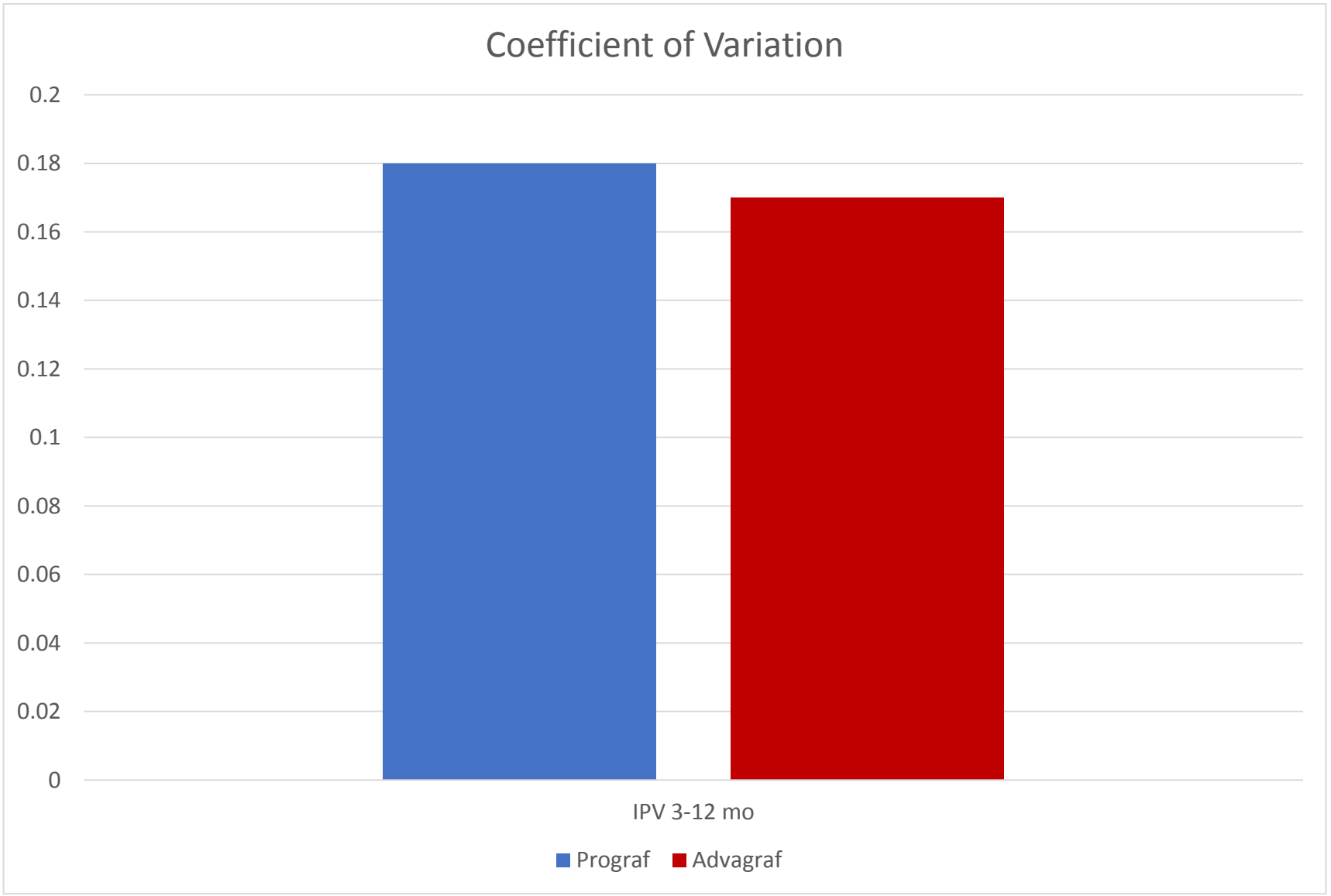
Variable	Prograf	Advagraf	P-Value
C_0 Month 3	8.9 ± 3.4	8.1 ± 2.7	0.150
C_0/Dose Month 3	3.4 ± 4.1	2.8 ± 2.7	0.240
C_0 Month 6	8.8 ± 3.7	7.7 ± 2.6	**0.075**
C_0/Dose Month 6	2.9 ± 2.1	2.9 ± 2.1	0.989
C_0 Month 12	8 ± 2.9	8.8 ± 3.7	0.232
C_0/Dose Month 12	3.5 ± 2.7	2.7 ± 1.6	0.121


Tacrolimus Level
13.0
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
Day 3
Day 7
Month 1
Month 3
Month 6
Month 12
factor1
Prograf vs Advagraf
prograf
advagraf


Tacrolimus Level / Dose
5.20
5.00
4.80
4.60
4.40
4.20
4.00
3.80
3.60
3.40
3.20
3.00
2.80
2.60
2.40
2.20
2.00
1.80
1.60
1.40
1.20
1.00
.80
Month 3
Month 6
Month 6
factor1
Prograf vs Advagraf
prograf
advagraf

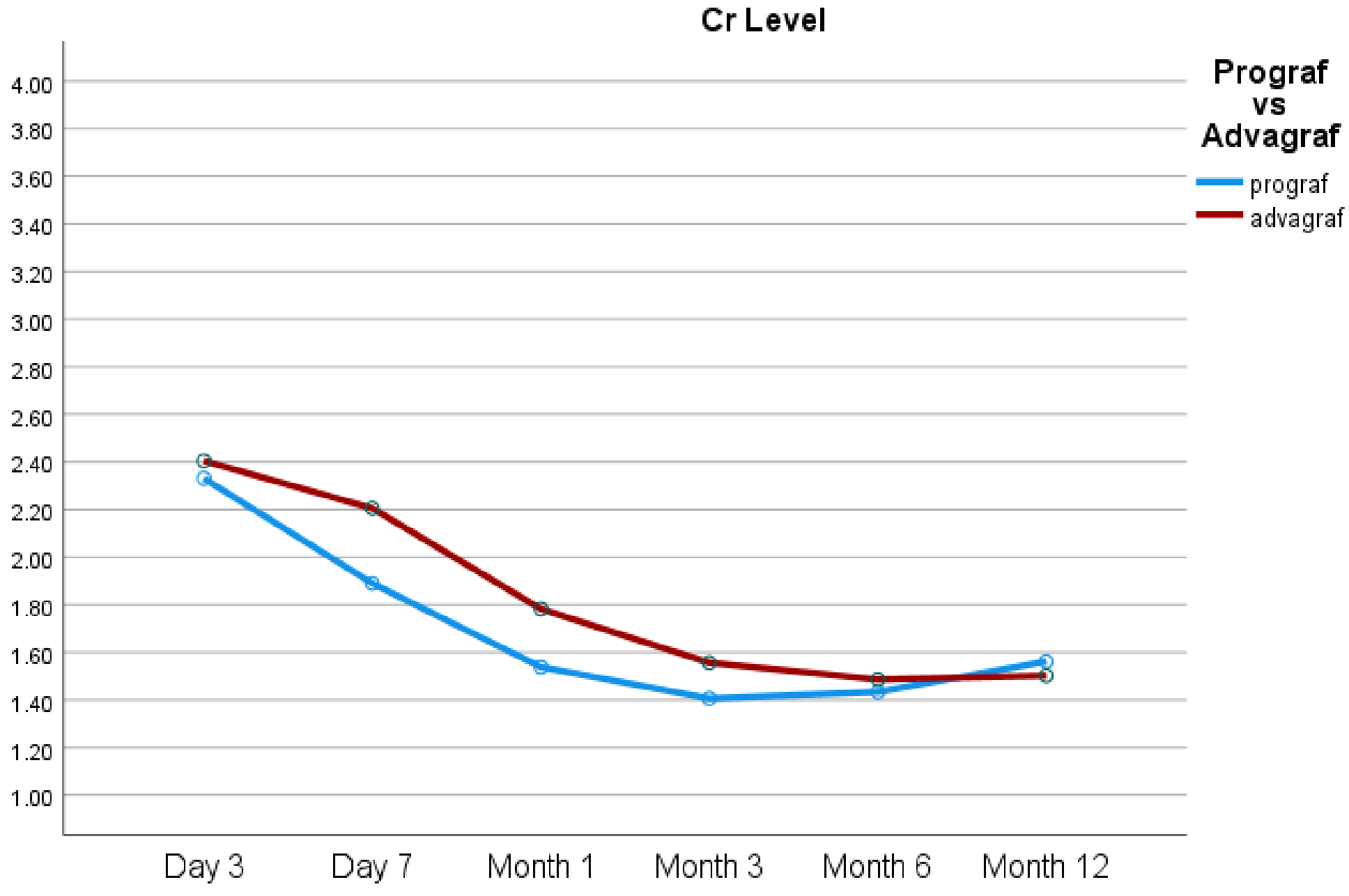
Intrapatient Variability (IPV)

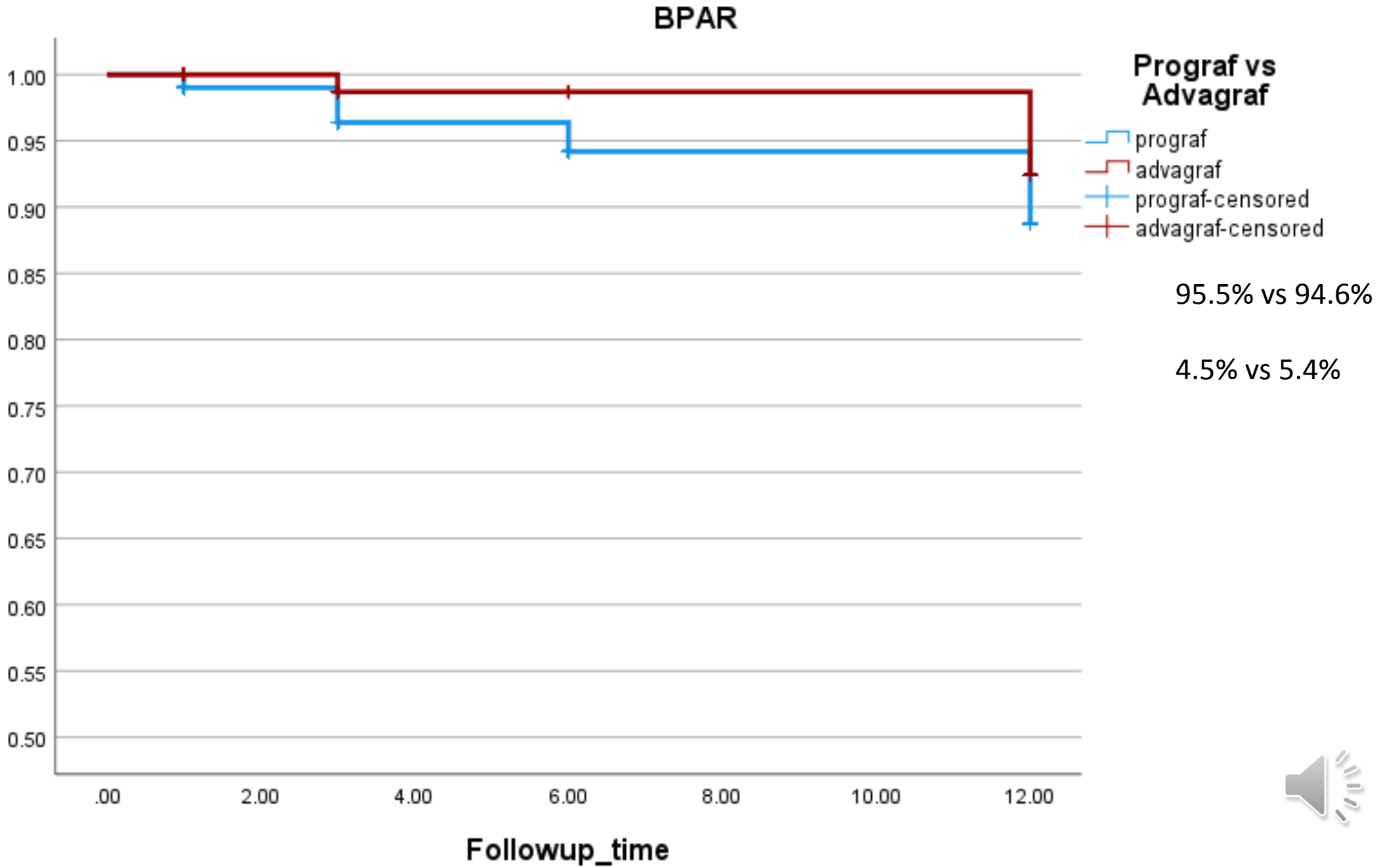
Variable	Prograf	Advagraf	P-Value
IPV Month 3 to Month 12	0.18 ± 0.13	0.17 ± 0.13	0.689


Coefficient of Variation
0.2
0.18
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
IPV 3-12 mo
Prograf
Advagraf

Allograft Function

Variable	Prograf	Advagraf	P-Value
Cr Day 3	2 ± 1.6	2.2 ± 1.8	0.213
Cr Day 7	1.8 ± 1.5	2.1 ± 1.9	0.120
Cr month 1	1.6 ± 1	1.8 ± 1.3	0.179
Cr month 3	1.6 ± 1	1.6 ± 1.3	0.694
Cr month 6	1.5 ± 0.9	1.5 ± 1	0.908
Cr month 12	1.5 ± 1.1	1.4 ± 0.68	0.436


Cr Level
4.00
3.80
3.60
3.40
3.20
3.00
2.80
2.60
2.40
2.20
2.00
1.80
1.60
1.40
1.20
1.00
Day 3
Day 7
Month 1
Month 3
Month 6
Month 12
Prograf vs Advagraf
prograf
advagraf

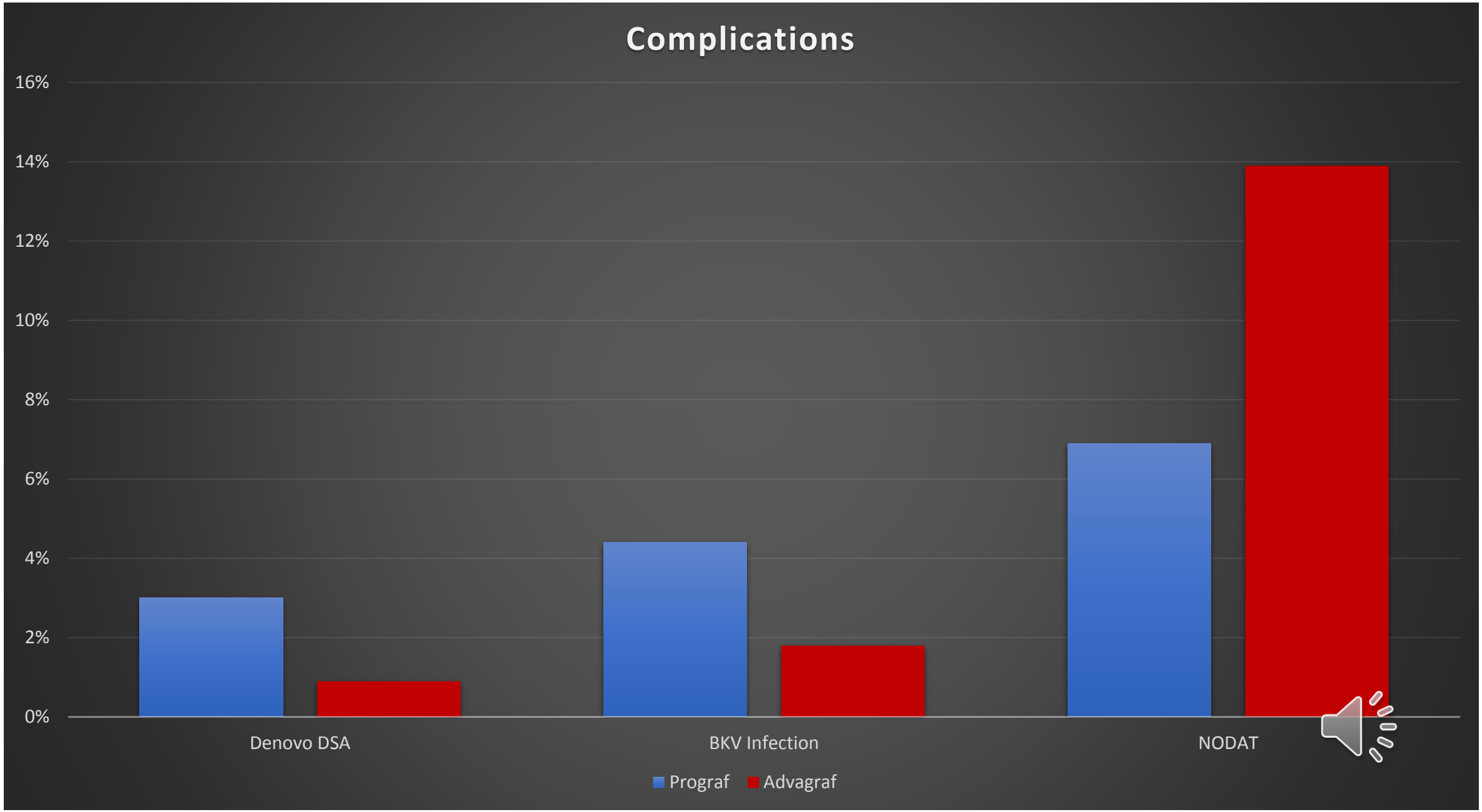


95.5% vs 94.6%

4.5% vs 5.4%

Adverse Events

Variable	Prograf	Advagraf	P-Value
Denovo DSA	3%	0.9%	0.238
BKV Infection	4.4%	1.8%	0.339
NODAT	6.9%	13.9%	0.097


Complications
16%
14%
12%
10%
8%
6%
4%
2%
0%
Denovo DSA
BKV Infection
NODAT
Prograf
Advagraf

Conclusion

- The **dose-normalized drug levels (Level-to-Dose ratio)** were overall lower with **Advagraf**, with statistically significant differences on **day 7** and **day 30**.
- **Intra-patient variability (IPV)** was **lower** in the **Advagraf** group compared to Prograf, although the difference did not reach statistical significance.
- There were **no statistically significant differences** between the two groups regarding **acute rejection**, **BK virus infection**, **de novo DSA and NODAT.**
- However, the incidence of **acute rejection** and **de novo DSA** tended to be lower in the Advagraf group.
- **In summary, Advagraf demonstrated a more favorable pharmacokinetic profile, while clinical outcomes were comparable, with a trend toward fewer immunological events in the Advagraf group**