Benefit: Risk Assessment

Edmund J. Lewis, M.D.

Muehrcke Professor of Nephrology
and Director of the Section of Nephrology
Rush Medical College, Chicago, IL

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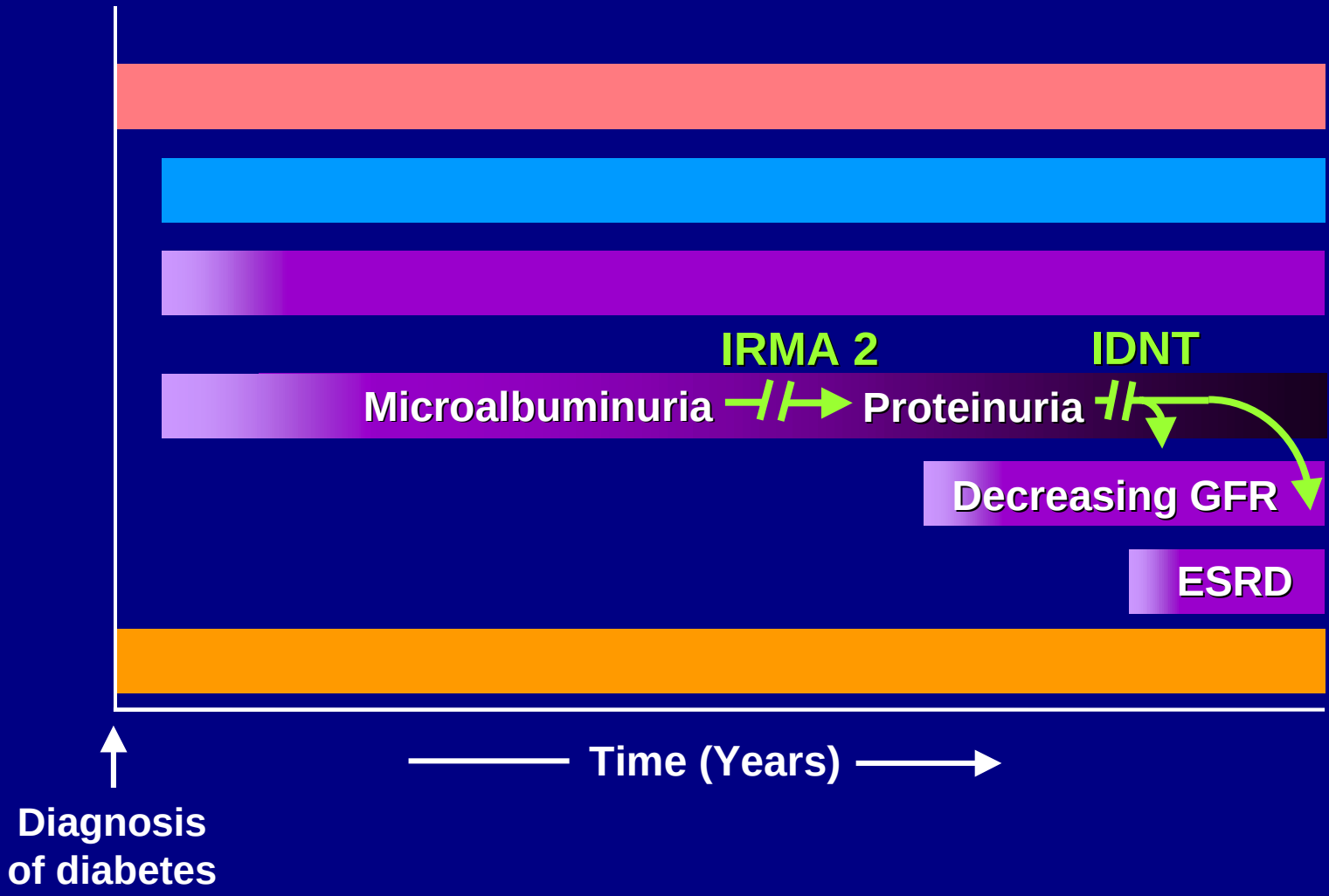
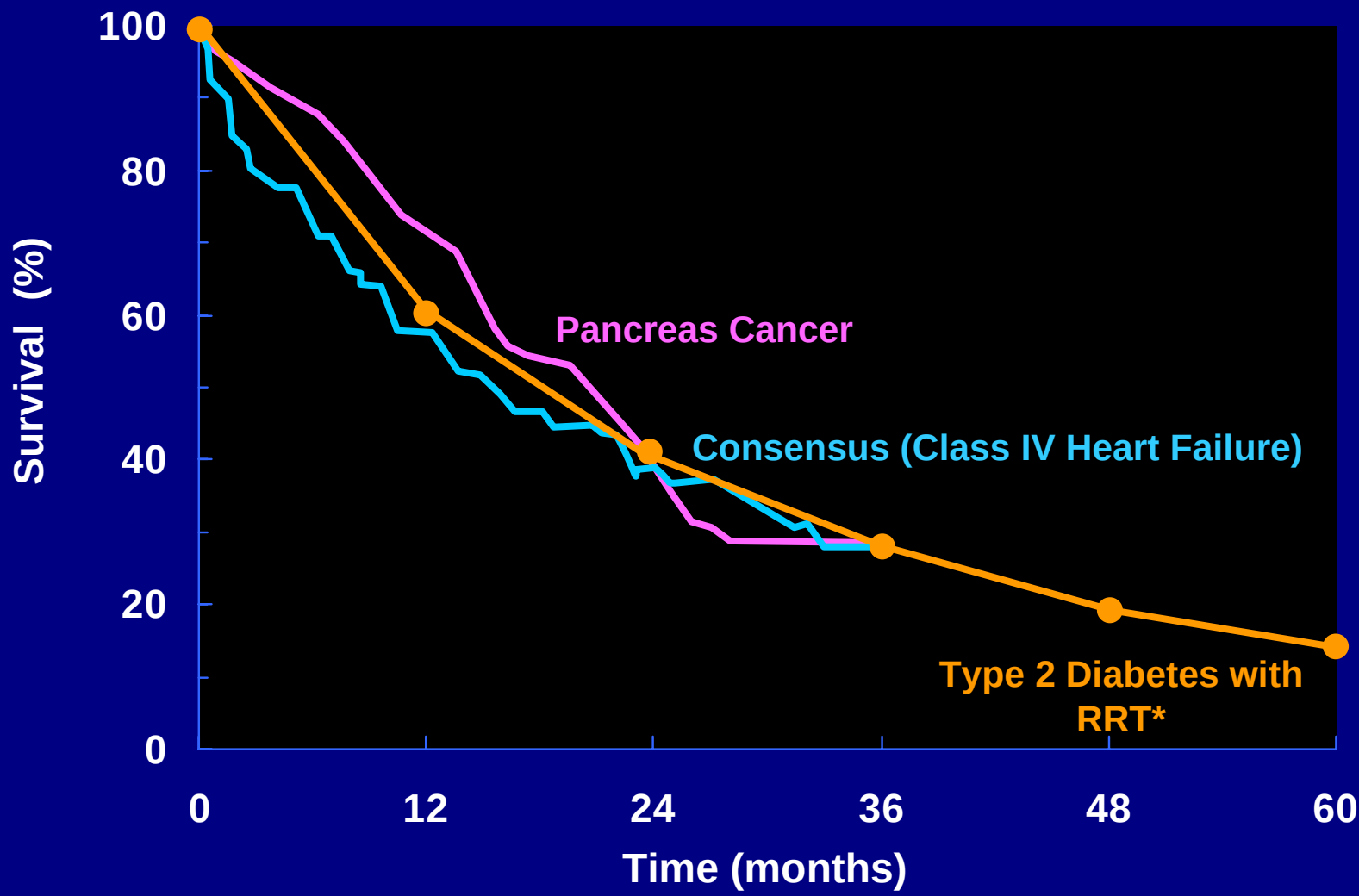
Natural History of Type 2 Diabetic Nephropathy

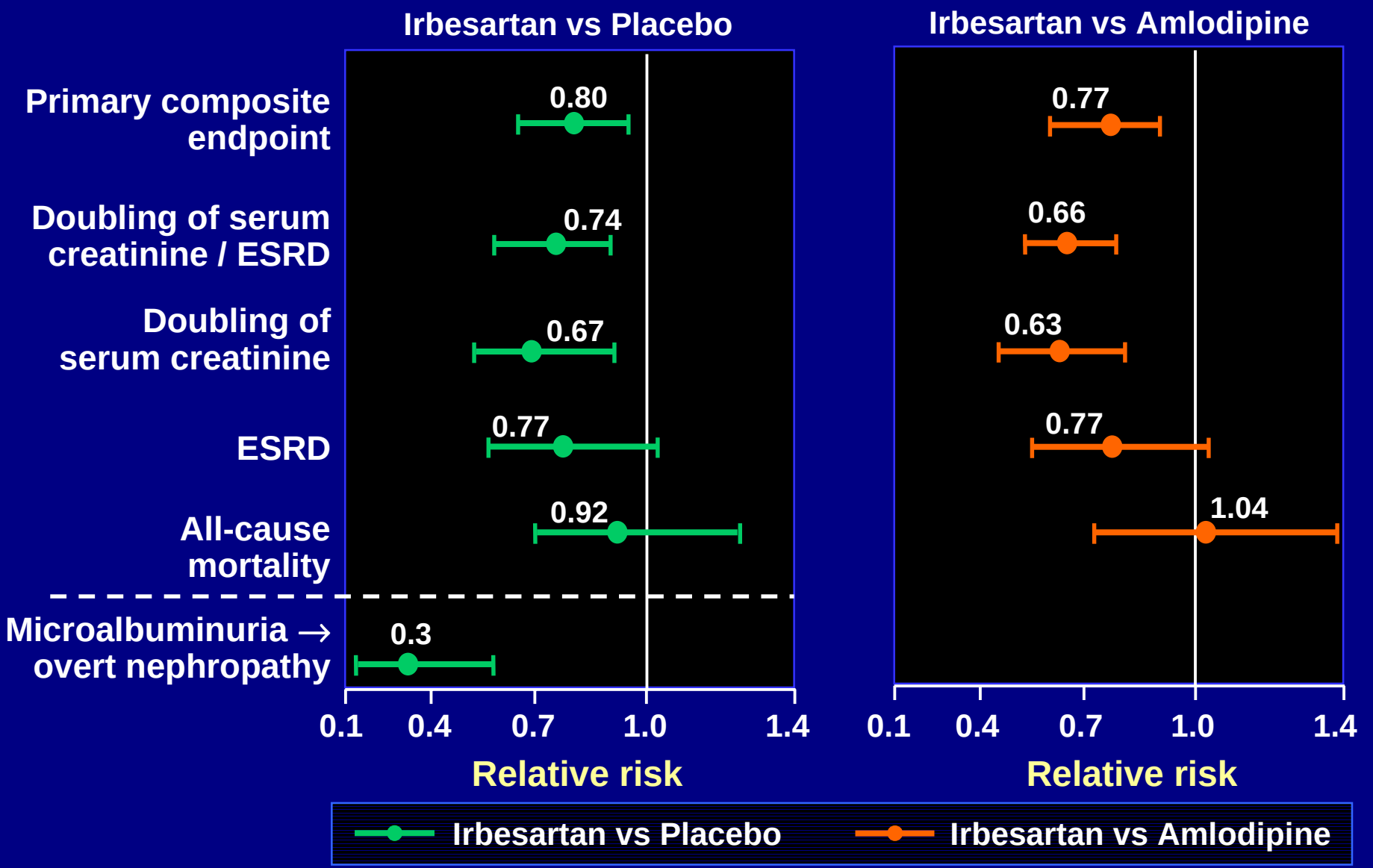


Survival of Patients With Type 2 Diabetes Receiving Renal Replacement Therapy (RRT)



* Hirschl, MM *et. al.,* Am. J. Kidney Dis. 1992; 20: 564-568

Summary of Efficacy of Irbesartan in Type 2 Diabetic Nephropathy



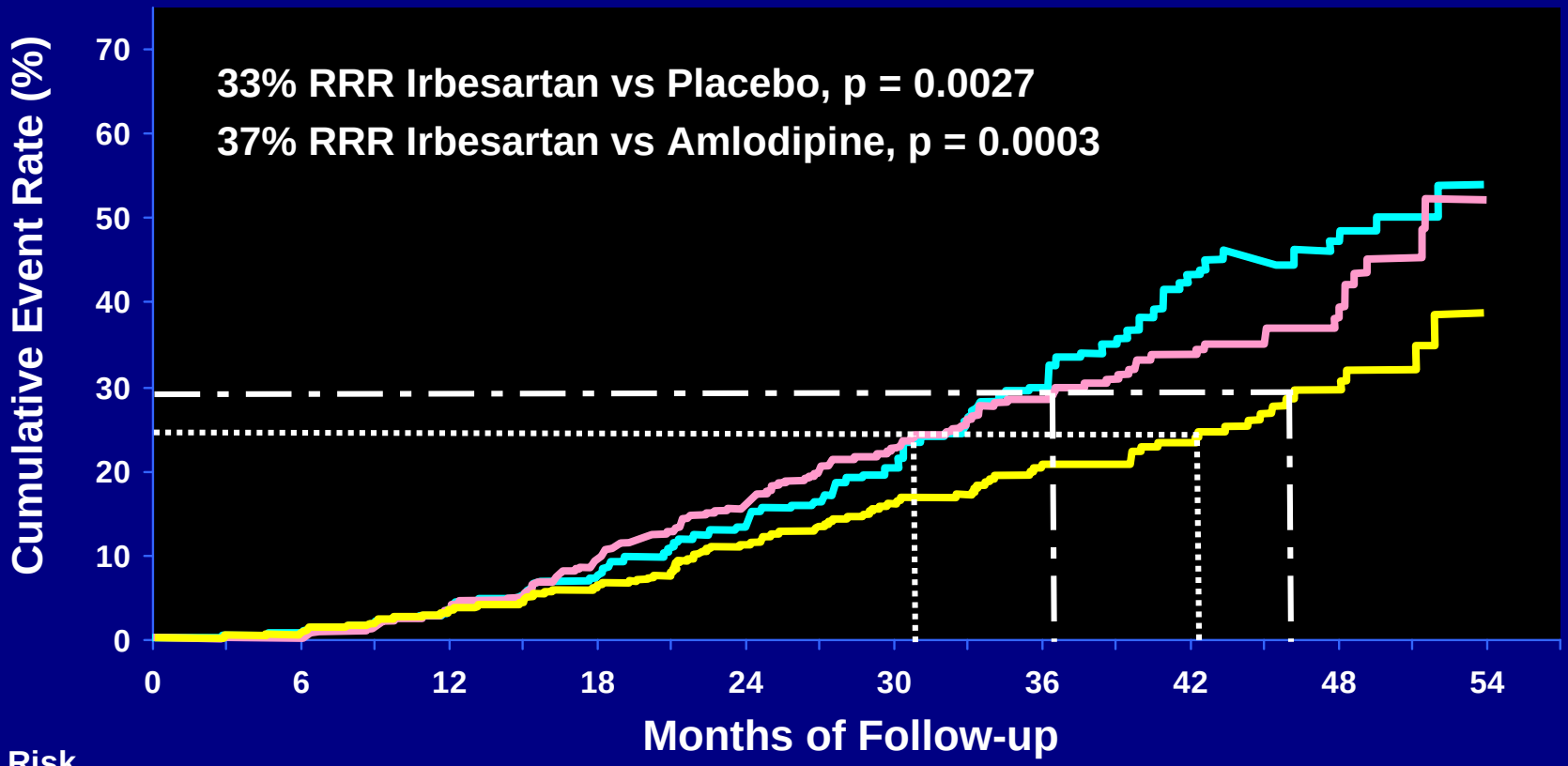
IDNT: Occurrence of ESRD or Death Based Upon Doubling of Serum Creatinine

Endpoints[a]	Number (%) of Subjects		
	Serum Creatinine Doubled[b] N = 377	Serum Creatinine Not Doubled N = 1,338	Total N = 1,715
ESRD[c]	202 (53.6)	85 (6.4)	287 (16.7)
Death	50 (13.3)	213 (15.9)	263 (15.3)

[a] The endpoints are not mutually exclusive
[b] Includes 55 subjects who had simultaneous doubling of SCr and Scr ≥ 6.0
[c] Includes Scr ≥ 6.0, dialysis, or transplant

IDNT: Time to Doubling of Serum Creatinine

Figure S.10.1B

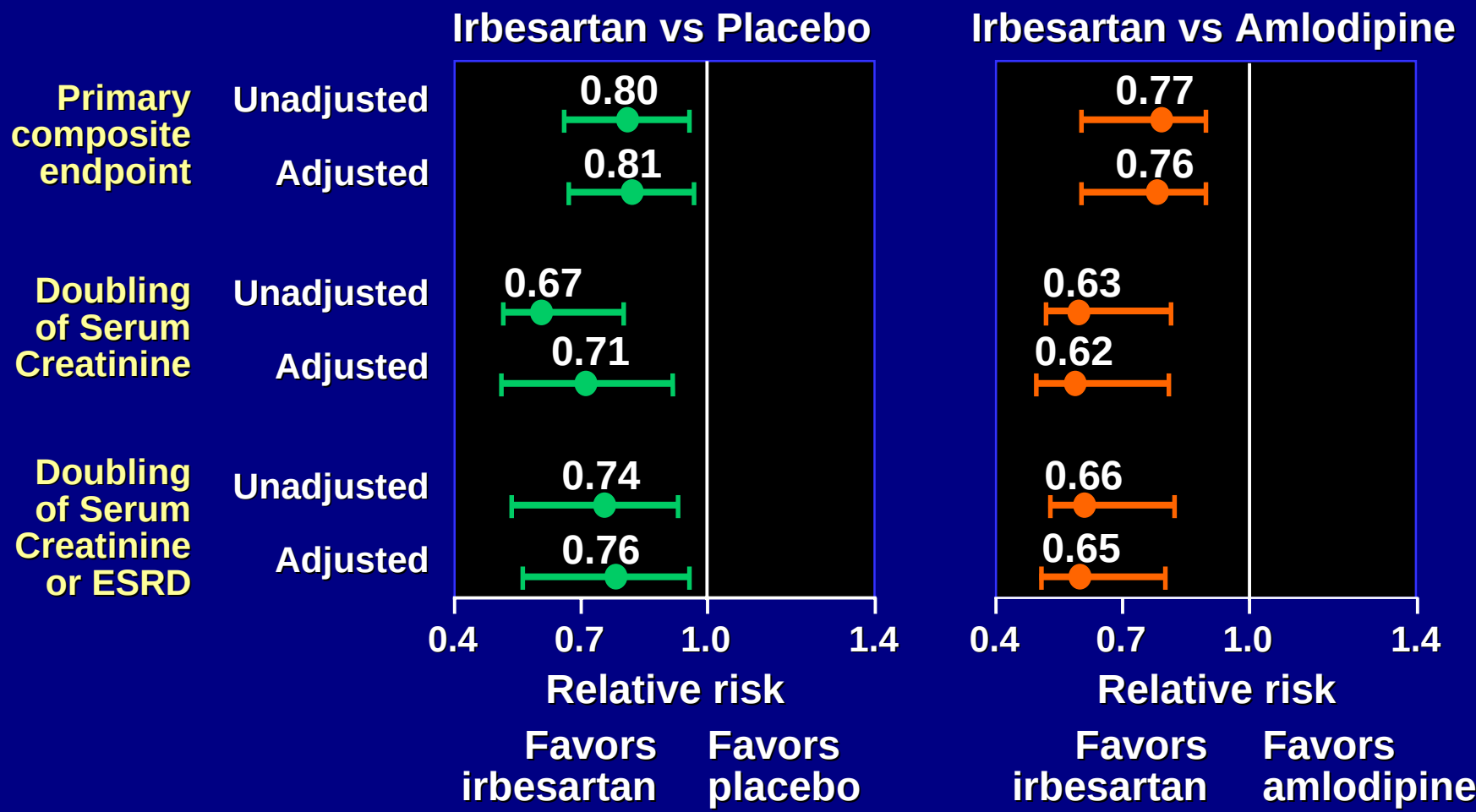


No. at Risk

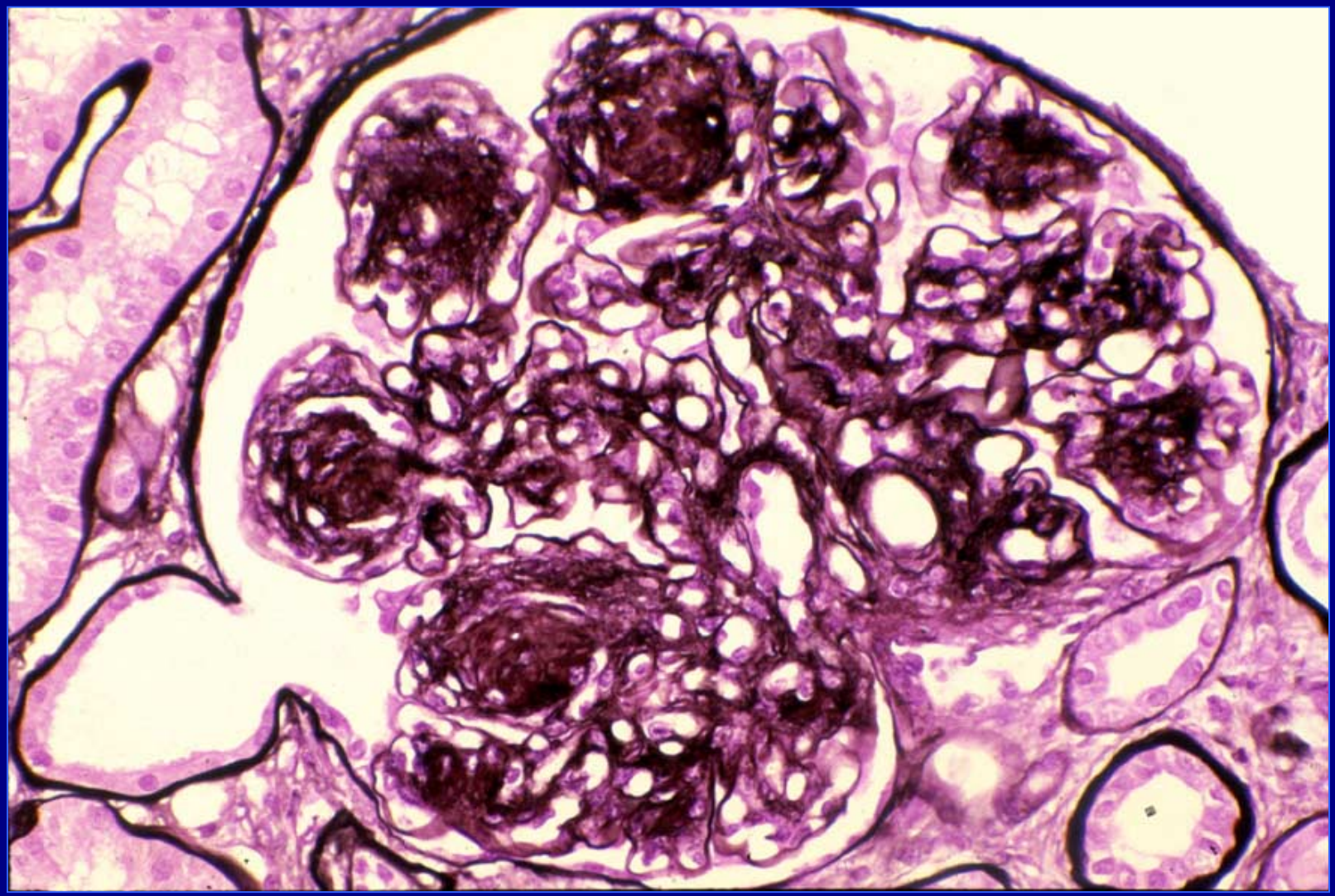
Placebo	569	529	485	438	366	260	177	111	51	2
Irbesartan	579	536	496	457	371	275	194	137	62	5
Amlodipine	567	516	477	440	362	265	171	109	42	6

Dataset: Randomized Subjects, ITT analysis

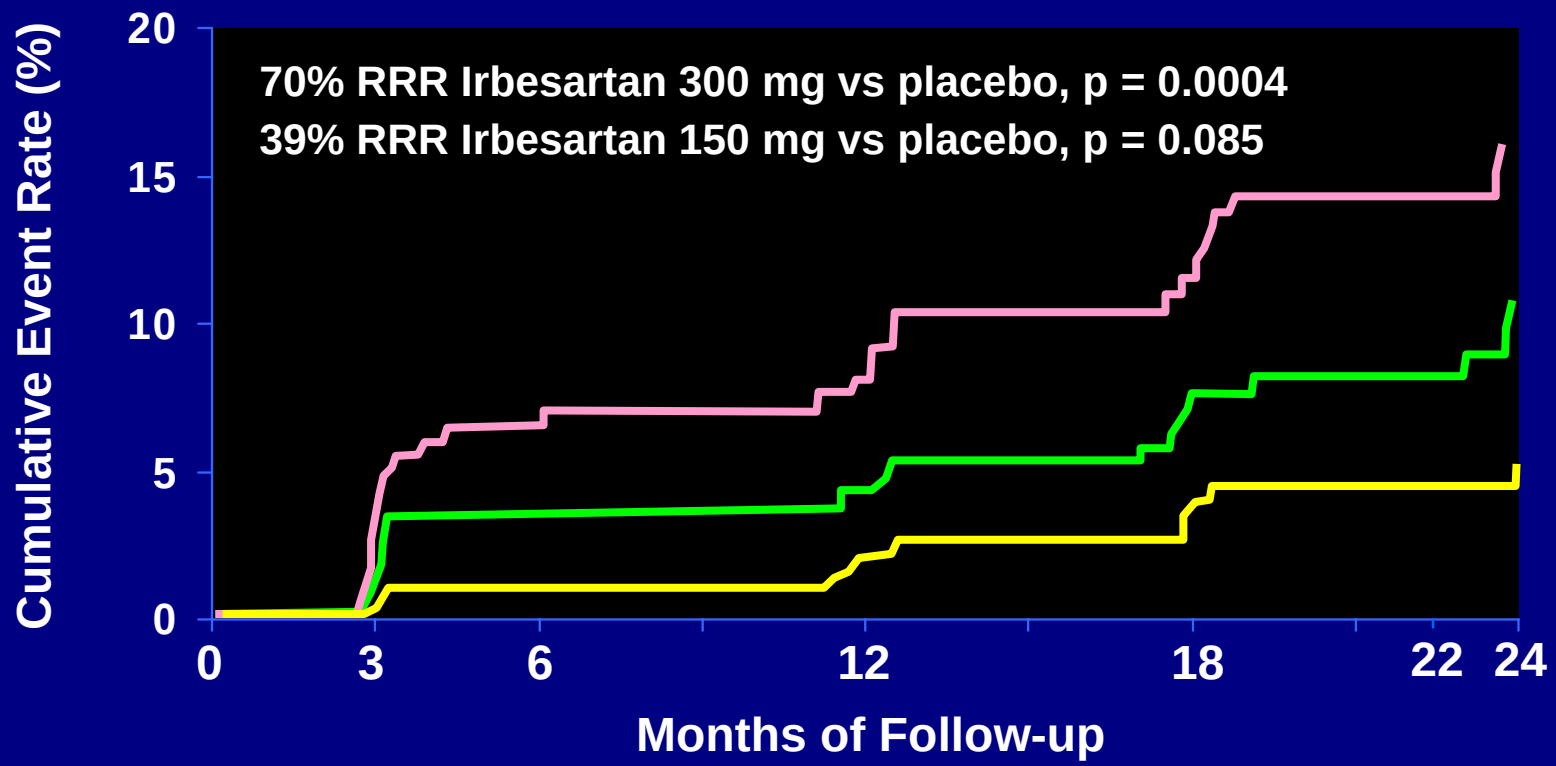
IDNT: Primary Endpoint – Adjustment for Blood Pressure



Glomerular Histopathology in Type 2 Diabetic Nephropathy



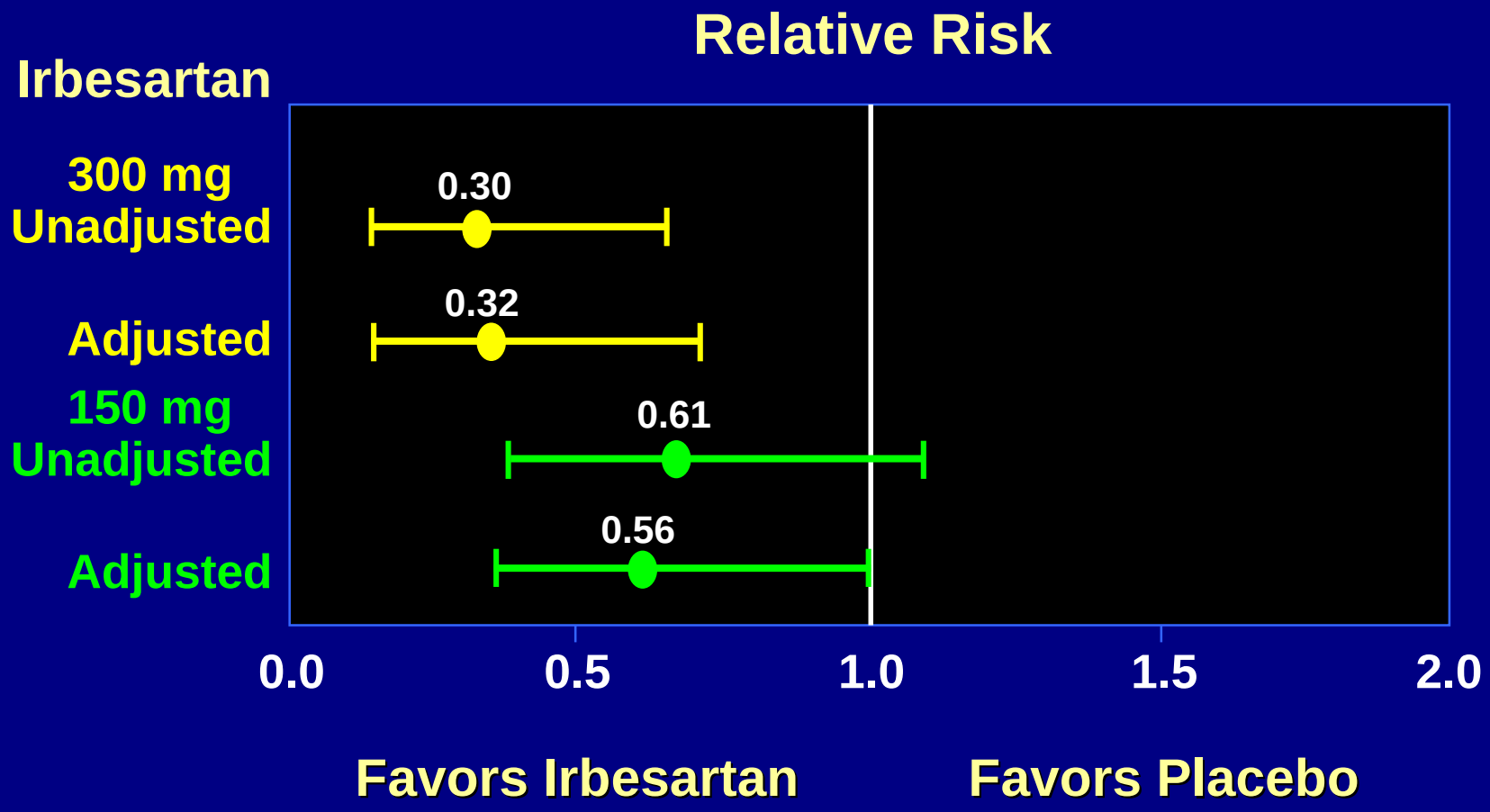
IRMA 2: Primary End Point – Time to Development of Overt Nephropathy



No. at Risk

Placebo	201	201	164	154	139	129	36
Irbesartan 150 mg	195	195	167	161	148	142	45
Irbesartan 300 mg	194	194	180	172	159	150	49

IRMA 2: Primary Endpoint – Adjustment for Blood Pressure



Conclusion Regarding the Renoprotection Hypothesis

Irbesartan retards the progression of both early and overt nephropathy in type 2 diabetes mellitus by a mechanism which is independent of blood pressure control

Numbers Needed to Treat

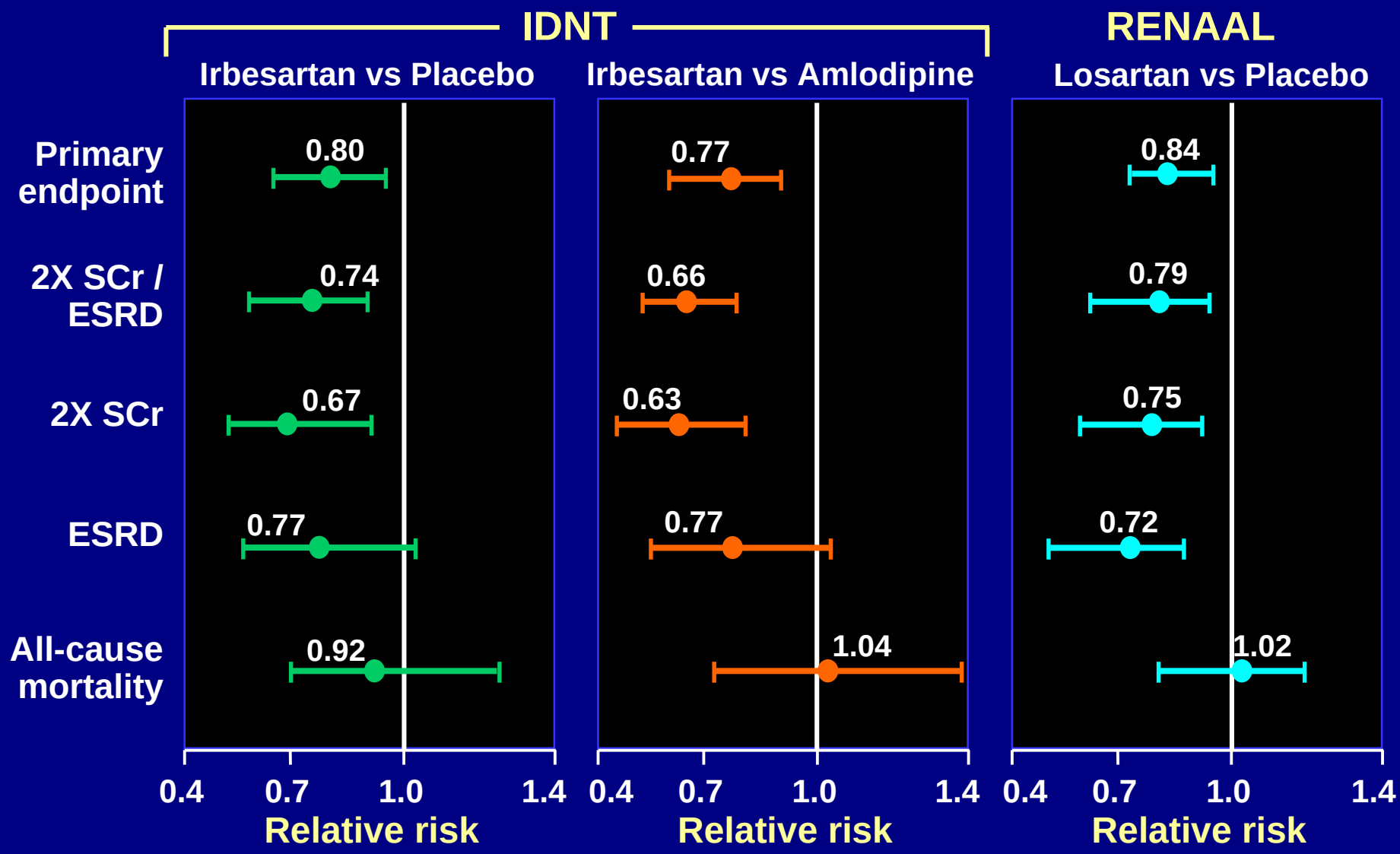
Drug	Population	Event	Duration of Treatment	NNT*
Irbesartan	Overt nephropathy	Doubling of serum creatinine-ESRD	3 years	15
Irbesartan	Microalbuminuria	Overt nephropathy	2 years	10

* Defined as the number of patients that need to be treated to prevent one event.

Recent Clinical Trials Demonstrating Renoprotection of ARBs in Type 2 Diabetic Renal Disease

- Lewis, E.J., *et. al.*, Renoprotective Effect of the Angiotensin-Receptor Antagonist Irbesartan in Patients with Nephropathy due to Type 2 Diabetes. NEJM 2001; 345: 851-860. - (IDNT)
- Parving, H-H, *et. al*., The Effect of Irbesartan on the Development of Diabetic Nephropathy in Patients with Type 2 Diabetes. NEJM 2001; 345: 870-878. - (IRMA2)
- Brenner, B.M. *et. al.*, Effect of Losartan on Renal and Cardiovascular Outcomes in Patients with Type 2 Diabetes and Nephropathy. NEJM 2001; 345: 861-869. - (RENAAL)

Comparison of Clinical Studies in Overt Type 2 Diabetic Nephropathy



SCr = Serum Creatinine

Benefit: Risk Assessment

- Collectively, these results demonstrate the renoprotective benefits of irbesartan across the continuum of diabetic renal disease
- The benefit: risk assessment favors the use of irbesartan across the continuum of diabetic renal disease