

Final Diagnoses

1. *Pneumocystis jirovecii* pneumonia
2. HIV/AIDS

Teaching point: timing of ART initiation

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Early Antiretroviral Therapy Reduces AIDS Progression/ Death in Individuals with Acute Opportunistic Infections: A Multicenter Randomized Strategy Trial

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- **ACTG A5164 (2009):** RCT of early vs. delayed ART initiation in AIDS-related OI in 282 patients
- 283 subjects (May 2003 - August 2006): 85% men, median age 38, diverse (37% black, 36% Hispanic, and 23% white), median CD4 29 (70% had CD4 < 50), **63% of patients had PCP.**
- **Primary endpoint:** 3-level, ordered, categorical variable: (1) alive without AIDS progression and with HIV VL < 50 copies/mL (best outcome) at week 48; (2) alive without AIDS progression and with detectable HIV VL (i.e. VL \geq 50 copies/ml) at week 48 (intermediate outcome); and (3) AIDS progression or death (worst outcome) at any time.

Table 2. Study Efficacy and Safety Outcomes over 48 weeks by Strategy Arm.

Outcome	Total	Early	Deferred	p-value
No Endpoint Information	36 (12.8%)	18 (12.8%)	18 (12.8%)	
Primary Endpoint				
AIDS Progression/Death	54 (19.1%)	20 (14.2%)	34 (24.1%)	
Plasma Viral Load >50 copies; no progression*	98 (34.8%)	54 (38.3%)	44 (31.2%)	
Plasma Viral Load <50 copies; no progression	130 (46.1%)	67 (47.5%)	63 (44.7%)	0.215 ^a
Secondary Endpoints				
AIDS Progression/Death	54 (19.1%)	20 (14.2%)	34 (24.1%)	0.035 ^b
HIV VL % <50 copies at 48 wks (ITT analysis)	143 (51%)	71 (50%)	72 (51%)	0.48 ^c
CD4 count at 24 weeks (median change from baseline) (IQR)	+115 (+71--+180)	+118 (+75--+186)	+104 (+66--+171)	0.22 ^c
CD4 count at 48 weeks [median change from baseline] (IQR)	+187 (+106--+269)	+187 (+95--+268)	+187 (+124--+271)	0.50 ^c
Safety Outcomes				
Had at least one ART Switch or interruptions,	104 (39%)	59 (42%)	45 (35%)	0.26 ^d
IRIS Confirmed	20 (7.1%)	8 (5.7%)	12 (8.5%)	0.49 ^d
Laboratory Adverse Events Grades 2–4	192 (68%)	90 (64%)	102 (72%)	0.16 ^d
Clinical Adverse Events Grades 2–4	130 (46%)	61 (43%)	69 (50%)	0.40 ^d
Subjects with Hospitalization	106 (38%)	55 (39%)	51 (36%)	0.71 ^d
Median Hospital Days (among hospitalizations)	5 (2–10)	5 (2–10)	6 (2–10)	0.79 ^c

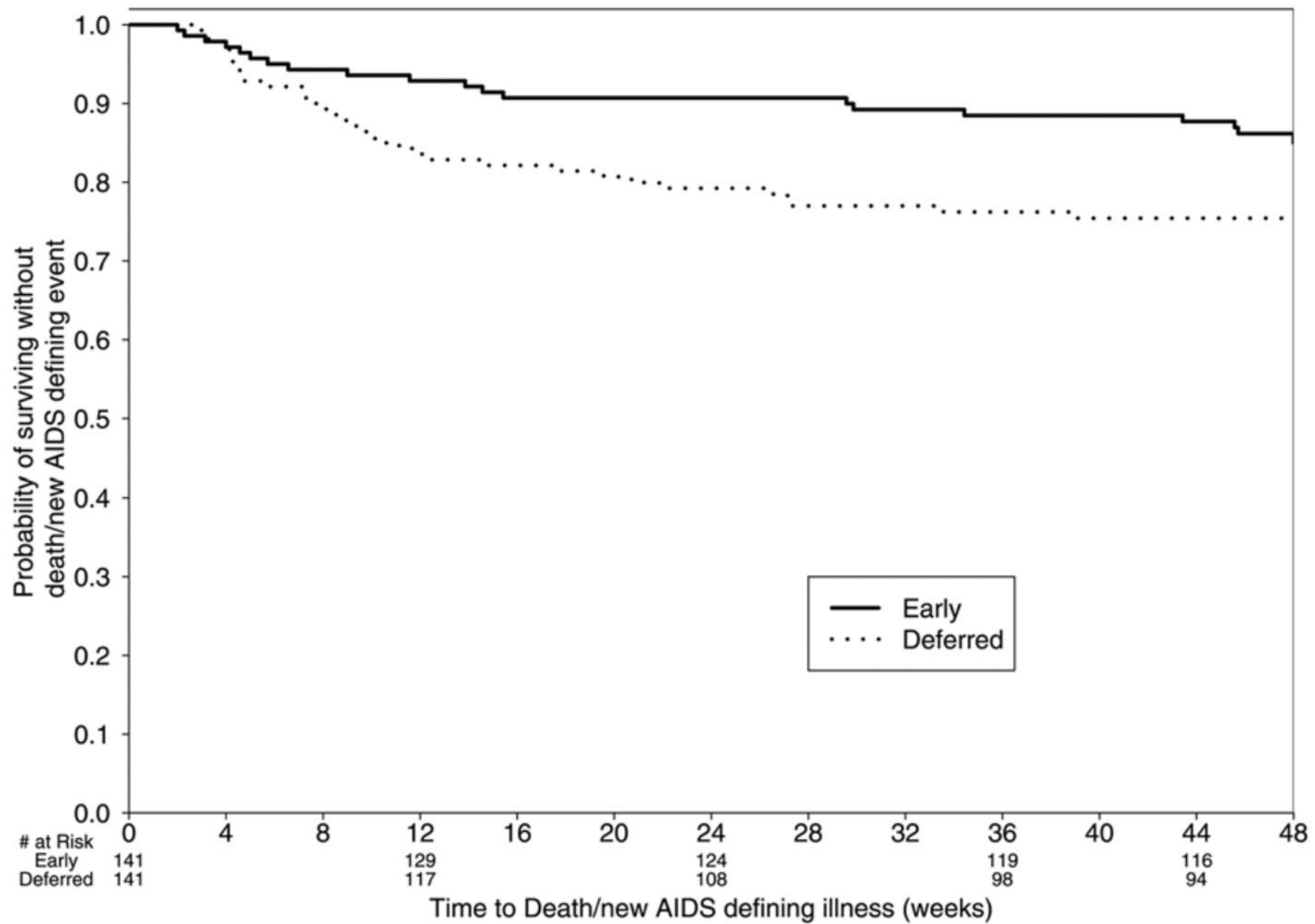


Figure 3. Time to AIDS progression or death. HR=0.53 Early versus Deferred ART [95%CI 0.30–0.92 p=0.023].
doi:10.1371/journal.pone.0005575.g003